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Cellular mechanisms that establish HIV-1 latency in CD4+ T cells and the potential for their manipulation as a therapeutic strategy

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CELLULAR MECHANISMS THAT ESTABLISH HIV-1 LATENCY IN CD4+ T CELLS AND THE POTENTIAL FOR THEIR MANIPULATION AS A THERAPEUTIC STRATEGY

by

MATTHEW GAGNE

B.A., Boston University, 2009

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Approved by

First Reader _____

Andrew J. Henderson, Ph.D.
Associate Professor of Medicine
Associate Professor of Microbiology

Second Reader _____

Suryaram Gummuluru, Ph.D.
Associate Professor of Microbiology

"Every great and deep difficulty bears in itself its own solution. It forces us to change our thinking in order to find it."

- Attributed to Niels Bohr, Ph.D.

Nobel Laureate, 1922

DEDICATION

For my parents, James and Monique Gagne, who introduced me to research.

For my mentors and classmates, who inspired me to persevere through my research.

For Myung-Eun, my life long research partner.

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CELLULAR MECHANISMS THAT ESTABLISH HIV-1 LATENCY IN CD4+ T CELLS AND THE POTENTIAL FOR THEIR MANIPULATION AS A THERAPEUTIC STRATEGY

MATTHEW GAGNE

Boston University School of Medicine, 2019

Major Professor: Andrew J. Henderson, Ph.D., Associate Professor of Medicine and Microbiology

ABSTRACT

Human Immunodeficiency Virus 1 (HIV-1) remains a significant public health concern due to the lack of a cure. In spite of anti-retroviral therapies, HIV-1 persists within infected cells as integrated transcriptionally silent proviruses. Re-activation after therapy interruption results in new HIV-1 replication. Attempts to clear this reservoir through the use of latency reversing agents by targeting cellular mechanisms that maintain HIV-1 in a latent state have been unsuccessful. In addition, subsets of latently infected cells exist within the reservoir that display differential capacities for provirus induction. In order to understand the nature of the reservoir and manipulate it therapeutically, more knowledge is needed regarding factors that bias a virus towards latency or replication at the time of infection.

Because multiple mechanisms that regulate HIV-1 transcription, including chromatin remodeling, transcription factor activation and polymerase pausing, are regulated by the T cell receptor (TCR), I hypothesized that signaling at the time of infection determines proviral fate. I transduced Jurkat cell lines and primary CD4+ T

cells with chimeric antigen receptors (CARs) that mimicked signaling from the TCR. These CARs spanned a 3-log range of binding affinities for their ligand, providing a tunable model. High levels of TCR stimulation during infection biased cells towards productive replication and the formation of an inducible latent reservoir. Examination of the mechanisms downstream from TCR signaling revealed that robust cellular activation led to a release of the repressor Negative Elongation Factor from the paused RNA Polymerase II, facilitating transcriptional elongation.

Because signaling determined the presence of repressive factors, I sought to manipulate the balance between latency and expression through recruitment of repressors to the HIV-1 provirus using a nuclease-deficient CRISPR Associated Protein 9 fused to a Krüppel Associated Box Domain. I screened a pool of guide RNAs that mediated transcriptional repression of HIV-1. Our lab discovered that guides bound to the HIV-1 Long Terminal Repeat prevented viral re-activation in an integrated cell model of HIV-1 latency.

The research presented here confirms my hypothesis that signals during infection have prolonged effects on latency reversal. I provide evidence that manipulation of these mechanisms represent therapeutic targets for cure efforts.

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AIDS ..... Acquired Immunodeficiency Syndrome

ANOVA ..... Analysis of Variance

AP-1 ..... Activator Protein 1

APC ..... Antigen-Presenting Cell

ART ..... Antiretroviral Therapy

BET ..... Bromodomain and Extra-Terminal Motif

BRD4 ..... Bromodomain-Containing Protein 4

BU ..... Boston University

CAR ..... Chimeric Antigen Receptor

cART ..... Combination Antiretroviral Therapy

dCas9 ..... Disabled (Nuclease-Deficient) CRISPR Associated Protein 9

CRISPR ..... Clustered Regularly Interspaced Short Palindromic Repeats

DSIF ..... DRB Sensitivity Inducing Factor

Efz ..... Efavirenz

ELISA ..... Enzyme-Linked Immunosorbent Assay

ESCRT ..... Endosomal Sorting Complexes Required for Transport

FDR ..... False Discovery Rate

γδ ..... Gammadelta T Cells

GFP ..... Green Fluorescent Protein

HATs ..... Histone Acetyltransferases

HDAC ..... Histone Deacetylase

HDACi ..... Histone Deacetylase Inhibitor

Her2 ..... Human Epidermal Growth Factor Receptor 2

HIV-1 ..... Human Immunodeficiency Virus 1

HMT ..... Histone Methyltransferase

HUSH ..... Human Silencing Hub

ITAM ..... Immunoreceptor Tyrosine-Based Activation Motif

Kap1 ..... KRAB-Associated Protein-1 (Trim28)

KRAB ..... Krüppel Associated Box Domain

LAT ..... Linker of Activated T Cells

Lck ..... Lymphocyte-Specific Protein Tyrosine Kinase

LRA ..... Latency Reversing Agent

LTR ..... Long Terminal Repeat

MAPK ..... Mitogen-Activated Protein Kinase

MHC ..... Major Histocompatibility Complex

NF-κB ..... Nuclear Factor Kappa-Light-Chain-Enhancer of Activated B Cells

NFAT ..... Nuclear Factor of Activated T Cells

Nef ..... HIV Negative Regulatory Factor

NELF ..... Negative Elongation Factor

PBMCs ..... Peripheral Blood Mononuclear Cells

PHA ..... Phytohaemagglutinin

PKC ..... Protein Kinase C

PLCγ1 ..... Phosphoinositide Phospholipase C Gamma 1

PMA ..... Phorbol Myristate Acetate

PrEP ..... Pre-Exposure Prophylaxis

PtdIns(4,5)P_2 ..... Phosphatidylinositol 4,5-Bisphosphate

P-TEFb ..... Positive Transcription Elongation Factor

RNAPII ..... RNA Polymerase II

SAHA ..... Suberanilohydroxamic Acid (Vorinostat)

SBHA ..... Suberoyl Bis-Hydroxamic Acid

scFv ..... Single-Chain Variable Fragment

Sh2 ..... Src Homology 2

SIV ..... Simian Immunodeficiency Virus

SP1 ..... Specificity Protein 1

Src ..... Proto-Oncogene Tyrosine-Protein Kinase Src

SWI/SNF ..... Switch / Sucrose Non-Fermentable

Tat ..... HIV Transactivator of Transcription

TCR ..... T Cell Receptor

TNFα ..... Tumor Necrosis Factor Alpha

VOA ..... Viral Outgrowth Assay

Vpr ..... HIV Viral Protein R

Vpx ..... HIV Viral Protein X

VSVG ..... Vesicular Stomatitis Virus Envelope Glycoprotein G

Zap70 ..... Zeta-Chain-Associated Protein Kinase 70

CHAPTER ONE: INTRODUCTION

The Emergence and Pathology of Human Immunodeficiency Virus-1

Human Immunodeficiency Virus-1 (HIV-1) was first reported in a notice from the Centers of Disease Control on June 5, 1981 (CDC, 1981). This medical newsletter, which identified an outbreak of *Pneumocystis* pneumonia among homosexual men in Los Angeles, quickly brought attention to the spread of a contagious immunodeficiency. The underlying immune dysfunction, Acquired Immunodeficiency Syndrome, would later be discovered to be caused by the virus now known as HIV-1 (Gallo and Montagnier, 2003).

HIV-1 evolved from SIV or Simian Immunodeficiency Virus (Ringler *et al*., 1987; Smith *et al*., 1988). SIV consists of several species-specific strains that circulate among non-human primates, usually resulting in minimal symptoms and long-term tolerance (Bostik *et al*., 2001). Cross-species jumps of these various strains from non-human primates into human hosts have led to the emergence of both HIV-1 and the related virus HIV-2. HIV-1 shares significant homology with the chimpanzee variant of SIV, known as SIVcpz, and most likely originated in central Africa in the first half of the 20th century (Gao *et al*., 1999). The HIV-1 major groups M, N, O, and P arose from separate evolutionary cross-over events from SIVcpz or SIVgor (gorilla) and required the acquisition of the ability to inhibit key human restriction factors, so named for the ability to restrict viral replication (Sauter and Kirchhoff, 2019). In particular, HIV-1 Group M, which evolved from SIVcpz, can robustly inhibit a key restriction factor, tetherin, and

thus constitutes the majority of viruses responsible for the current human pandemic (Sauter *et al.*, 2009)

HIV-1 spread to North America due to increased travel and globalized commerce in the mid-1900's. Once in the United States, the virus spread quickly among Haitian immigrants, men who have sex with men (MSM), and hemophiliacs, who were susceptible to infection due to their need for frequent blood transfusions (De Cock, Jaffe and Curran, 2012). Mass hysteria over both the source of AIDS as well as the mode of transmission led to a concerted effort by the National Institutes of Health, the Centers for Disease Control, and the Institut Pasteur in Paris to fund AIDS-related research. These experiments culminated in the landmark discovery of HIV-1 in 1983 as the causative agent of AIDS in North America and Europe by Luc Montagnier and Françoise Barré-Sinoussi (Barré-Sinoussi *et al*., 1983).

We now know that HIV-1 results in a depletion of the lymphocytic CD4+ T cell population. This weakens the adaptive immune response, rendering the host vulnerable to a wide variety of opportunistic infections (Frazer *et al*., 1986; Shearer *et al*., 1986). Early AIDS-identifying diseases included *Pneumocystis* pneumonia, Kaposi's sarcoma, and toxoplasmosis from *Toxoplasma gondii* (Pitchenik *et al*., 1983). With the advent of antiretroviral therapies or ART in 1986, remarkable progress has been achieved in preventing the onset of AIDS (Mitsuya *et al*., 1985). This progress was particularly enhanced with the design of combination therapy involving cocktails of inhibitors (Tisdale *et al*., 1993). However, in spite of cART, lifelong infection with HIV-1 still results in greater risk of cardiovascular disease, kidney failure, and neurocognitive

impairments (Freiberg *et al*., 2013; Guaraldi *et al*., 2011; Simioni *et al*., 2010). Patients experience permanent immune dysfunction, even after full viral suppression. Persistent exposure to viral antigens results in both immune exhaustion and constant inflammation (Hunt *et al*., 2003; French *et al*., 2009; Hatano *et al*., 2013). Antiretroviral therapies, while essential to prevent progression to AIDS, also cause a number of serious side effects including loss of bone density, gastrointestinal discomfort, and hypersensitivity (Güerri-Fernández *et al*., 2017; Santos *et al.*, 2017; Wu *et al.*, 2017).

The use of Truvada as pre-exposure prophylaxis (PrEP) beginning in 2012 has dramatically changed the trajectory of the HIV public health epidemic. Prescribing Truvada to high-risk populations has substantially reduced the spread of the virus (Grant *et al.*, 2010). However, neither cART nor PrEP has resulted in a cure for HIV-1 or the end of its transmission. In fact, although new infections of HIV-1 within the United States have plateaued, infection with HIV-1 is still a matter of much stigma and remains prevalent both in poorer regions of the southeastern United States (CDC, 2018) as well as Southeast Asia, Eastern Europe, and sub-Saharan Africa (Stuart *et al.*, 2018). Seventy percent of all HIV cases occur in sub-Saharan Africa where access to PrEP is extremely limited (Kharsany and Karim, 2016). Other groups that are still particularly susceptible to infection include MSM, sex-workers, IV-drug users, and minority women (CDC, 2018; UNAIDS, Guidance Note on HIV and Sex Work, 2019). Even with proper education and increased societal awareness, adherence to medication remains a major barrier to viral suppression. Thus, eradication of HIV-1 remains a significant challenge. The United Nations has prioritized a strategy, referred to as 90-90-90, in which the global medical

community aims to achieve 90% diagnosis of HIV, 90% ART-treatment among those diagnoses, and 90% viral suppression among those taking ART (Stover *et al.*, 2016). In tandem with this approach, there have been significant efforts to create a broad spectrum HIV-1 vaccine, but none of these strategies have so far completely prevented the spread of HIV-1 or led to a cure (Rerks-Ngarm *et al.*, 2009; Gray *et al.*, 2011). These factors all indicate that continued efforts must be made to eradicate HIV-1 and end both the terrible medical burden and social stigma caused by this virus. At the time of this publication, more than 35 million people have died from AIDS-related illnesses, including 1 million people in 2017 alone (UNAIDS, Global HIV & AIDS Statistics, 2019).

The Life Cycle of HIV-1

When HIV-1 enters the human body, it is presumably trafficked through the mucosa by antigen-presenting cells or APCs (Hladik *et al.*, 2007). These APCs, including dendritic cells, Langerhans cells, and macrophages, play an important role in bridging the innate and adaptive immune responses. They endocytose pathogens before trafficking them to the cell surface in conjunction with an MHC Class II complex (Roche and Furuta, 2015). This presentation along with secondary stimulation by cytokines or cell surface receptors can trigger a specific response in lymphocytes for which the epitope of interest acts as the cognate antigen.

Eventually, HIV-1 is delivered by APCs to the lymph nodes, where it spreads to various target cells including macrophages, dendritic cells, and the primary reservoir of

CD4+ T cells (Barré-Sinoussi *et al.*, 1983; Armstrong and Horne, 1984; Koenig *et al.*, 1986). The fact that HIV-1 can infect the APCs that present it to its various target cells highlight the dual role that can occur within dendritic cells and macrophages. Both direct infection and trans-infection through antigen presentation provide two routes through which HIV-1 can spread and highlight the importance of cell interactions to viral transmission (Cameron *et al.*, 1992; McDonald *et al.*, 2003). For dendritic cells, the differentiation state determines which of these routes can occur; for instance, trans-infection via CD169, a cell surface lectin, is associated with mature DCs (Puryear *et al.*, 2013).

HIV-1 target cells contain the necessary receptors for viral entry: CD4 and a coreceptor of CCR5 or CXCR4 (Feng *et al.*, 1996; Deng *et al.*, 1996; Dragic *et al.*, 1996). Founder viruses use CCR5 for viral entry and are referred to as R5-tropic. The progression to dual-tropic or X4-tropic viruses, which exclusively use CXCR4 for entry, is associated with both onset of AIDS and a depletion of R5-expressing cells (Connor *et al.*, 1997). This coreceptor switch does not occur in all HIV-infected patients.

The HIV-1 virion is spherical and marked by a limited number of glycoprotein envelope spikes (Zhu *et al.*, 2006). It consists of a lipid membrane derived from its previous host cell (Nguyen *et al.*, 2000) and contains an internal capsid harboring two copies of its genome as viral RNA (Chen *et al.*, 2009). In addition, it packages essential proteins for its replication, including reverse transcriptase, integrase, and its transcription factor Tat (Huang *et al.*, 1994; Bosso *et al.*, 2015; Kessl *et al.*, 2016). In addition, the viral accessory protein Vpr or Viral Protein R is also packaged and is required for robust

transcription in dendritic cells (Miller *et al.*, 2017). When the HIV-1 envelope binds to its appropriate receptors, it triggers fusion with the cell membrane (Maddon *et al.*, 1988). Fusion is thought to occur through a suggested series of intermediate steps, in which the outer glycoprotein trimer, referred to as gp120, engages with CD4. This allows the coreceptor binding site to become accessible; the HIV-1 fusion peptide then can interact with the target cell, forming a hairpin which pulls apart the cell membrane and facilitating the delivery of the virion (Chan and Kim, 1998; Wang H *et al.*, 2016).

Upon entry, HIV-1 unloads its capsid into the cell cytoplasm. Within the capsid, the RNA genome is reverse-transcribed into complementary DNA. Although the exact timing of reverse transcription has not yet been elucidated, it is believed that reverse transcription is completed by the time of nuclear entry (Rankovic *et al.*, 2017). Reverse transcription and capsid disruption is tightly correlated as revealed by a recent study by the Rousso lab at Ben-Gurion University using time-lapse atomic force microscopy to reveal that pressure inside the capsid increases due to the presence of newly formed DNA, eventually leading to capsid dissociation. After interaction with the nuclear pore complex, the capsid dissociates and the new cDNA is integrated into the host genome by the viral protein IN or integrase. HIV-1 is preferentially integrated into introns of actively transcribed genes (Han *et al.*, 2004), most of which would be located in euchromatic regions near the nuclear pore (Marini *et al.*, 2015; Acuthan *et al.*, 2018). The integration site is one of several key factors that determine whether HIV-1 is transcribed. At this point, HIV-1 expression is regulated not only by its transactivator Tat but also by the

general cellular factors that control gene transcription. This dependency on the host cell will be critical to the experiments I outline in this dissertation.

Once integrated, the viral genome is referred to as a provirus. This provirus is transcribed by the host RNA Polymerase II (RNAPII) for the purpose of making new viral RNA or transcribed and translated for the purpose of making new viral proteins. HIV-1 transcription is regulated by the binding of specific host factors to the 5' Long Terminal Repeat (LTR). The provirus is flanked on either end by an identical LTR that acts as the HIV-1 promoter (Patarca *et al.*, 1987). The presence of both LTRs is directly responsible for the capacity of reverse transcriptase to copy the entire genome including both the 5' and 3' untranslated regions. A number of transcription factors are known to bind to the HIV-1 LTR (and downstream sites) including NF-κB, AP-1, SP1, and NFAT (Calman *et al.*, 1988; Franza *et al.*, 1988; Garcia *et al.*, 1987; Lu *et al.*, 1991). The binding sites of these transcription factors, as well as the structure of the entire provirus, are shown in Figure 1.1. During the early stages of transcription, the HIV-1 transactivator Tat binds to a specific stem-loop structure in the nascent RNA referred to as the TAR region (Hauber and Cullen, 1988). During this process, Tat recruits the host factor P-TEFb or Positive Transcription Elongation Factor, which hyperphosphorylates the C-terminal domain of RNAPII. Phosphorylation results in transcriptional elongation and successful polymerase processivity (Napolitano *et al.*, 2000; Barboric *et al.*, 2001). P-TEFb cycles between an active state that is free to phosphorylate RNAPII and an inactive state in which it is sequestered by the 7SK RNA complex (Yang *et al.*, 2001). While the cellular signals that permit disassembly of the 7SK RNA – P-TEFb complex are not fully

elucidated, it has been shown that UV damage or MAPK signaling as a result of TCR engagement can activate P-TEFb (Yang *et al.*, 2001; Kim *et al.*, 2011). Therefore, successful HIV-1 transcription is regulated by both Tat fluctuations and P-TEFb activity (Weinberger *et al.*, 2005). In addition, the use of dual-fluorescence viruses that contain both inducible and constitutive reporters has indicated a more general role for cellular activation on productive infection (Duverger *et al.*, 2009; Chavez, Calvanese and Verdin, 2015). Cells with high basal levels of NF-κB are biased towards viral replication and away from transcriptional repression (Dahabieh *et al.*, 2014).

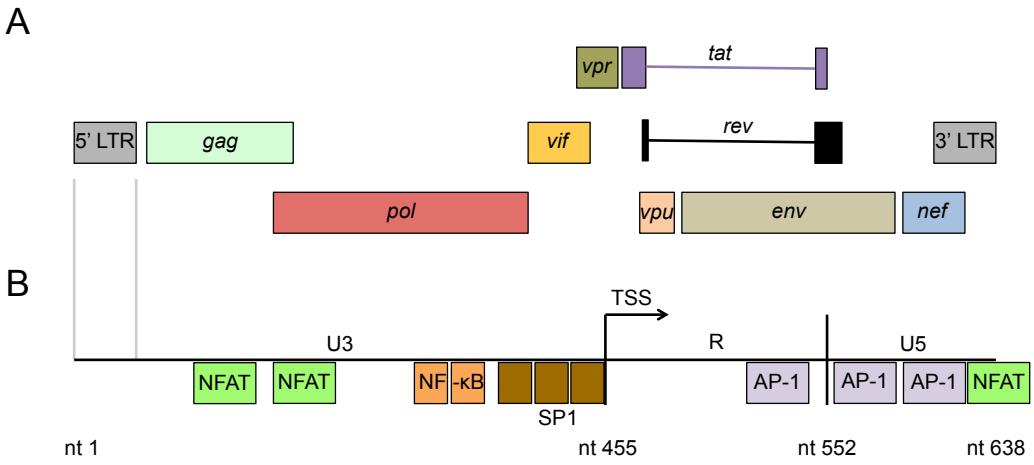

Figure 1.1: Binding sites of a select number of key transcription factors to the HIV-1 LTR. (A) HIV-1 proviral genome including both the 5' and 3' LTR's. (B) Detailed diagram of 5' LTR including binding sites of a select number of key transcription factors, transcriptional start site (referred to as TSS), and locations of U3, R, and U5 regions. This figure adapted from (Colin and Van Lint, 2009).

An additional block to HIV-1 replication occurs at the level of splicing. Because HIV-1 encodes its genome as a polycistronic RNA, efficient splicing is required for full expression of all viral products (Purcell and Martin, 1993; Emery *et al.*, 2017). The first

RNAs to emerge from the nucleus are fully spliced and contain the transcripts for HIV-1 Rev and HIV-1 Tat. This is followed by partially spliced transcripts that encode for the accessory proteins and the viral envelope. Finally, unspliced RNA enters the cytoplasm, resulting in both new copies of the viral genome along with the HIV-1 Gag and Pol polyproteins (Stoltzfus, 2009). Because only fully spliced transcripts are exported through normal cellular mechanisms, both the partially spliced and unspliced RNAs require the HIV-specific Rev-dependent export pathway (Fischer *et al.*, 1995).

While a subset of the unspliced RNA remains untranslated as viral RNA, the remaining transcripts must be translated by the cellular ribosome. Together, the viral capsid, various accessory factors, and the newly synthesized genomic RNA converge at the cellular membrane, where they bud to form a new virion (Sundquist and Kräusslich, 2012). The assembly at the lipid surface requires binding between PtdIns(4,5)P_2 and the matrix peptide of the Gag polyprotein (Saad *et al.*, 2006). The virion then co-opts the cellular ESCRT pathway due to indirect interactions between ESCRT factors and the HIV-1 p6 region of Gag to mediate scission from the cellular membrane (Sette *et al.*, 2016). In doing so, the virus acquires its outer lipid leaflet from the host cell. Further maturation by HIV-1 protease results in production of various Gag and Pol proteins, including, but not limited to, matrix (MA), capsid (CA), nucleocapsid (NC), reverse transcriptase (RT), integrase (IN), and protease (PR) (Swanstrom and Wills, 1997). Further rearrangements due to binding between these various proteins and movements of capsid into a conical structure results in the formation of a newly infectious particle,

capable of undergoing additional rounds of infection (Frank *et al.*, 2015). A depiction of the life cycle of HIV-1 is shown (Figure 1.2).

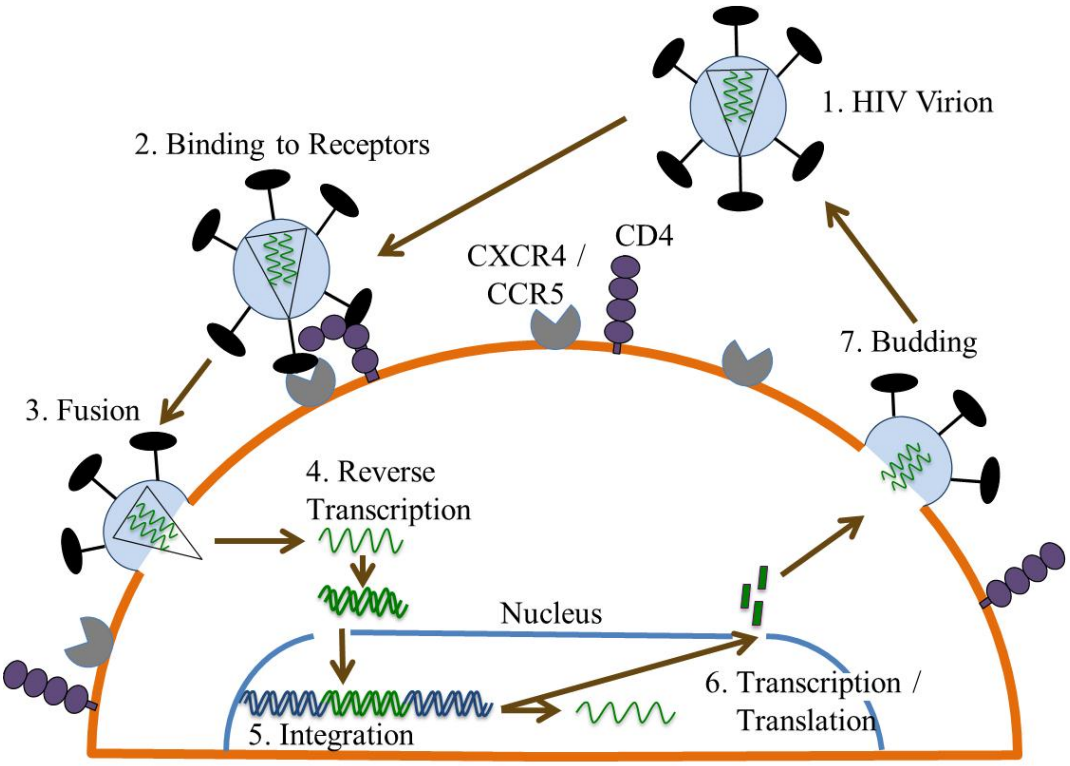

Figure 1.2: Life cycle of HIV-1. Major steps of the HIV-1 life cycle are shown, with emphasis placed on the stages where the virus is under the control of host cell machinery, including transcription / translation.

HIV-1 Latency

Biology and Model Systems

When the development of cART resulted in the suppression of viremia below the limit of detection, it was thought that a complete absence of viral replication would allow the host immune system to eradicate HIV-1 since infected cells will eventually undergo apoptosis due to either the cytopathic effects of the virus or clearance by NK cells and

CD8+ T cells (Koup *et al.*, 1994; Petravic *et al.*, 2014). If these infected cells were simultaneously blocked from producing new infectious particles, then a short course of ART would theoretically be sufficient to eliminate HIV-1 infection. However, in the years following the widespread use of ART, not one patient has achieved a cure through this mechanism (Chun *et al.*, 1997). In fact, after decades of antiretroviral treatments, even a short interruption of medication results in a predictable rebound of viremia as depicted in Figure 1.3 (Van Lint, Bouchat and Marcello, 2013). This is due primarily to the persistence of silent proviruses in long-lived memory CD4+ T cells.

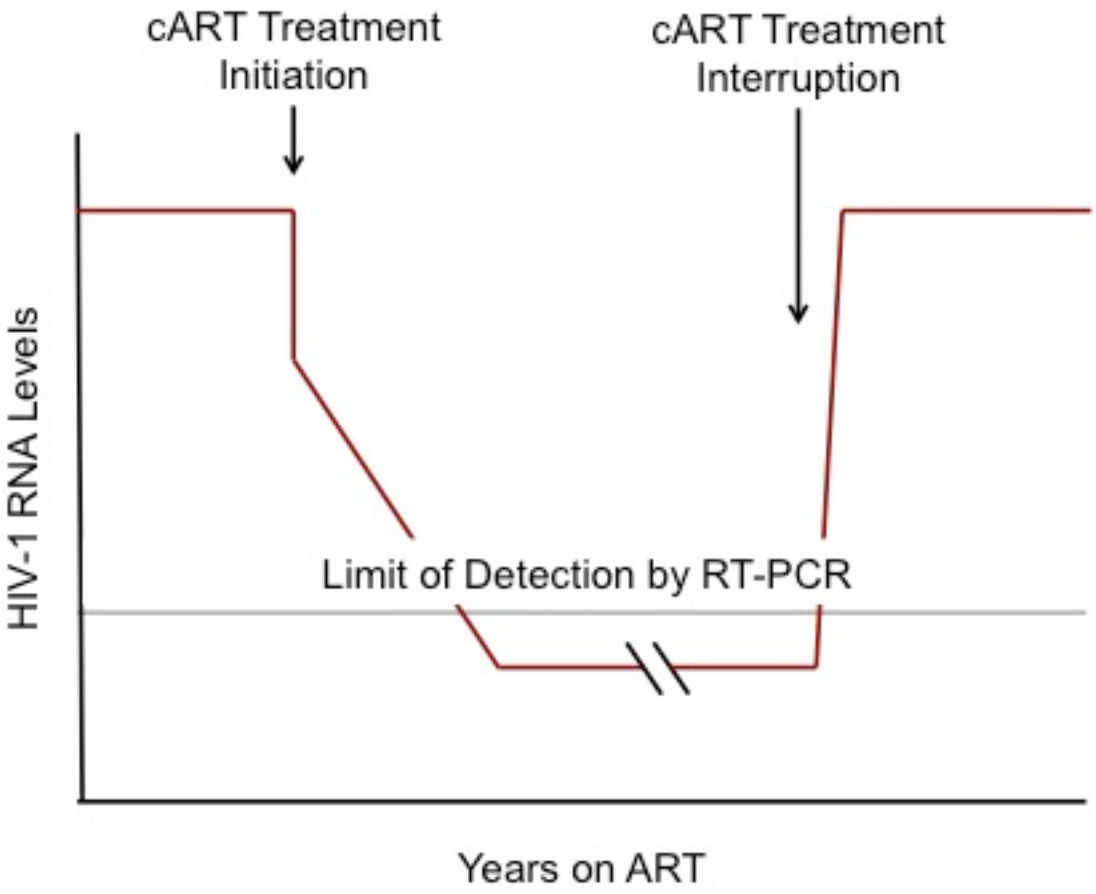

Figure 1.3: HIV-1 rebounds after cART interruption. Depiction of patient viral RNA levels as measured by RT-PCR both before and after antiretroviral therapy. Figure based on (Van lint, Bouchat and Marcello, 2013).

As a component of the adaptive immune system, CD4+ T cells and their progeny clones survive long-term and form the basis of immunological memory (Rogers, Dubey and Swain, 2000; Boyman *et al.*, 2009). If HIV-1 is integrated into these cells and if these cells do not produce any viral products that could be recognized by the immune system, the virus can evade detection. This phenomenon, known as HIV latency, forms the primary barrier to a cure for HIV-1. Like any normal cellular gene, HIV-1 can be either expressed or repressed. This repression thus prevents viral spread but also shields infected cells from antiviral immunity (Finzi *et al.*, 1997). The HIV-1 latent reservoir is also maintained by clonal proliferation of latently infected cells, which has been shown to allow for cellular duplication without viral re-expression (Wang *et al.*, 2018).

Our understanding of the mechanisms which maintain HIV-1 in a latent state derive from a number of *in vitro* models of HIV-1 latency as well as analysis of cells removed *ex vivo* from patients on ART. Among patients with full viral suppression, latent provirus has been discovered primarily in resting memory CD4+ T cells. These include both transitional memory and central memory subsets (Chomont *et al.*, 2009). PCR analysis has confirmed that roughly 1 in 1000 target resting cells are latently infected, but it is estimated that only 1 in 1,000,000 target cells contain an inducible latent provirus that can easily be re-activated as measured by the viral outgrowth assay or VOA (Ho *et al.*, 2013). To perform the VOA, researchers remove peripheral blood mononuclear cells (PBMCs) and culture them in limiting dilution along with target cells for HIV-1. The PBMCs are then reactivated with phytohaemagglutinin or PHA, which although highly

toxic, is a gold standard for latency reactivation *in vitro*. HIV-1 expression is then measured by p24 ELISA (Siliciano and Siliciano, 2005).

Although latent HIV-1 has been isolated primarily in CD4+ T cells and is most widely studied within this population, it is important to note that this is not the only cellular reservoir for latent provirus. Gammadelta or γδ T cells have been described as a target for HIV-1 infection and a source of rebounding virus following treatment interruption. γδ T cells have an important role in modulating the immune system and assisting other cell types, especially at barrier sites including the skin and mucosa (Paul *et al.*, 2014). Although less than 10% of γδ T cells are CD4+ *in vivo*, HIV-1 still requires the expression of CD4 in order to bind (Imlach *et al.*, 2003). HIV-1 can be isolated from γδ T cells in patients infected with HIV-1 on ART (Soriano-Sarabia *et al.*, 2015). Therefore, more information is needed regarding the potential contribution of γδ T cells to HIV-1 persistence.

Macrophages can also be infected by HIV-1 (Koenig *et al.*, 1986) and form a viral reservoir during prolonged ART. This has been identified both in humanized mouse models and in SIV-infected primates (Honeycutt *et al.*, 2017; Avalos *et al.*, 2017). Microglia, in particular, may contribute to HIV-1 persistence (Llewellyn *et al.*, 2018). However, when humanized myeloid only mice (containing human myeloid cells and human B cells) were infected with HIV-1 and given ART 5 weeks later, just 1/3 of all mice harbored latent virus (Honeycutt *et al.*, 2017). The fact that the majority of mice were not latently infected is supportive of the fact that CD4+ T cells, and not macrophages, are the primary reservoir for latency.

Because CD4+ T cells are the primary source for rebounding virus, most model systems that reproduce HIV-1 latency in a laboratory environment use primary CD4+ T cells or CD4+ T cell lines (Table 1.1). The first attempts to model HIV-1 latency were performed in A3.01 (Folks *et al.*, 1989) and Jurkat cells (Jordan, Bisgrove and Verdin, 2003) by the Fauci and Verdin laboratories. Cells with integrated virus but no clear RNA or protein production were isolated after multiple rounds of flow cytometry or reverse transcriptase activity assays. While these cells are useful for comparisons of various latency reversing agents (LRAs), they fail to adequately incorporate all of the mechanisms that contribute to HIV-1 latency *in vivo*. For instance, the A3.01 cell model, which resulted in creation of the ACH-2 line, has a defective TAR element that accounts for its propensity for latency (Emiliani *et al.*, 1996).

Other models use primary cells and attempt to either artificially prolong cell survival or infect specific types of cells known to harbor latent proviruses. The Siliciano model, for instance, uses the cell survival factor Bcl-2 to prevent cellular apoptosis (Kim *et al.*, 2014), while the O'Doherty / Greene model uses the slight perturbation caused by spinoculation to enhance viral integration into resting cells (Swiggard *et al.*, 2005; Lassen *et al.*, 2012). The Lewin model requires chemokine signaling (Saleh *et al.*, 2007), while the Planelles model directly infects certain subsets of memory cells (Bosque and Planelles, 2009).

Commonly Used Models of HIV-1 Latency			
Model	**Parental Cell**	**Mechanism to Enrich for Latency**	**References**
ACH-2 (Fauci)	A3.01	Defective TAR Element	Folks *et al.*, 1989 Emiliani *et al.*, 1996
J-Lat (Verdin)	Jurkat	Multiple Rounds of Cell Sorting to Isolate TNFα – Sensitive Silent Proviruses	Jordan, Bisgrove and Verdin, 2003
O'Doherty / Greene	Primary CD4+	Spinoculation	Swiggard *et al.*, 2005 Lassen *et al.*, 2012
Lewin	Primary CD4+	Chemokine Signaling (CCL19 and CCL21)	Saleh *et al.*, 2007
Planelles	Primary CD4+	Enrichment of Central Memory Cells / Polarization Towards Th1 and Th2	Bosque and Planelles, 2009
Siliciano	Primary CD4+	Transduction of Bcl-2	Kim *et al.*, 2014

Table 1.1: Commonly used models of HIV-1 latency. Models are listed along with methods for enrichment of latently infected cells.

Using these models to gain insights into the transcriptional regulation of HIV-1, a model has emerged in which multiple mechanisms regulate viral expression including epigenetic regulation, recruitment of key transcription factors, and RNAPII pausing. A primary determinant of viral reactivation in latently infected cells is a positioned nucleosome just downstream from the HIV-1 transcriptional start site, known as nuc-1 (Verdin, Paras and Van Lint, 1993). This nucleosome appears to be remodeled during transcriptional elongation (Van Lint *et al.*, 1996). The chromatin structure is opened through the addition of acetyl groups by HATs or histone acetyltransferases, many of which are recruited by transcription factors that are induced upon T cell signaling and bind the HIV-1 LTR, including NF-κB and AP-1 (Thierry *et al.*, 2004). In contrast, the

association of histone deacetylases or HDACs with HIV-1 inhibits transcription (Williams *et al.*, 2006). In addition, the chromatin remodeling complex SWI/SNF can directly remodel nuc-1, creating a transcriptional block or allowing for polymerase processivity (Mahmoudi *et al.*, 2006; Rafati *et al.*, 2011). These alternative roles are still being explored, but evidence exists that the binding to nuc-1 of specific variants of SWI/SNF, referred to as BAF and PBAF, are responsible.

Latency is associated with a lack of histone acetylation (He and Margolis, 2002) and premature polymerase pausing. This pausing has been identified in both the Henderson and Karn laboratories to be associated with the presence of the host repressive factors Negative Elongation Factor (NELF) and DRB Sensitivity Inducing Factor (DSIF) with RNAPII (Zhang, Klatt, Gilmour and Henderson, 2007; Jadlowsky *et al.*, 2014). These proteins prohibit RNAPII from proceeding downstream and ultimately recruit a third factor, Pcf11, which is known to cleave the nascent RNA, repressing HIV-1 transcription (Zhang, Klatt, Henderson and Gilmour, 2007). NELF and DSIF are both regulated by P-TEFb, which modulates their interactions with RNAPII through phosphorylation (Ping and Rana, 2001; Fujinaga *et al.*, 2004). Phosphorylated NELF can no longer bind the polymerase, while phosphorylated DSIF transitions into an activating factor that proceeds downstream with RNAPII. The HIV-1 protein Tat plays a key role in this process due to its ability to recruit P-TEFb to RNAPII once it is bound to the HIV-1 TAR region (Ping and Rana, 2001).

Each cell model system of latent HIV-1 has its advantage, although they often recapitulate only specific features of the entire latent reservoir. They exaggerate different

mechanisms that contribute to latency in order to create a large population of latently infected cells. These models are not optimal for understanding how latency is established at the time of HIV-1 infection. In particular, we do not know what signals are required for productive infection or the establishment of the reservoir. However, these cell models have been useful tools for identifying and exploring possible LRAs.

"Shock and Kill"

Based on the limited knowledge of the mechanisms that maintain latent HIV-1, several researchers proposed the use of LRAs to eradicate the viral reservoir. These LRAs were designed to prevent deacetylation of nuc-1 or to enhance release of P-TEFb, promoting HIV-1 expression; this would allow infected cells to be recognized and cleared by the immune system. Even if full reactivation of every integrated provirus was not achieved, a functional cure was originally thought to be possible through this process, known as "shock and kill" (Hamer, 2004).

Initial LRAs were histone deacetylase inhibitors or HDACi's, including valproic acid, which prevent the removal of acetyl groups from open and accessible nucleosomes. Valproic acid was already in use as an epilepsy therapeutic and was fast-tracked for HIV-1 clinical trials (Ylisastigui *et al.*, 2004). One clinical trial indicated that valproic acid was capable of inducing a 75% reduction in the amount of inducible latent proviruses by the VOA (Lehrman *et al.*, 2005). In spite of promising early results using valproic acid, there is now contradictory evidence regarding whether valproic acid can actually reduce

the number of inducible latent proviruses, and no clinical trial has shown an effect on the size of the entire DNA viral load (Archin *et al.*, 2008; Sagot-Lerolle *et al*., 2008; Archin *et al*., 2010; Routy *et al*., 2012).

Other HDACi's under consideration include SAHA or its analog SBHA. While SAHA can reactivate latent HIV-1 in HIV-infected cell lines such as J-LATs (based on Jurkat cells) and even has been shown to induce HIV-1 RNA expression in *ex vivo* PBMCs (Contreras *et al*., 2009; Reuse *et al*., 2009; Archin *et al*., 2009; Barton *et al.*, 2016), it has failed to reduce the amount of total HIV-1 DNA in clinical trials (Elliott *et al*., 2014; Barton *et al.*, 2016). Other studies have failed to detect any significant increases in the amount of HIV-1 RNA expression within *ex vivo* patient samples after stimulation with either valproic acid or SAHA (Blazkova *et al.*, 2012). As a result of these conflicting studies, the use of HDAC inhibitors as single latency reversing agents is no longer central to the "shock and kill" strategy of HIV-1 eradication.

Other LRAs being explored are known to target different mechanisms that maintain latent HIV-1. These include histone methyltransferase inhibitors (Bernhard *et al*., 2011; Bouchat *et al*., 2012; Friedman *et al*., 2011; Boehm *et al.*, 2017), DNA methyltransferase inhibitors (Kauder *et al*., 2009; Blazkova *et al*., 2009; Friedman *et al*., 2011), and protein kinase C activators. PKC agonists, in particular, have shown synergy with other LRAs, indicating that multiple pathways may have to be engaged in order to achieve a clinically relevant level of latency reversal (Bartholomeeusen *et al*., 2013; Dar *et al*., 2014).

In addition, JQ1 is being explored as a potential LRA (Banerjee *et al*., 2012; Bartholomeeusen *et al*., 2012; Zhu *et al*., 2012). It is hypothesized that JQ1, a BET bromodomain inhibitor, functions by targeting BRD4, which is known to bind P-TEFb (Bisgrove *et al*., 2007; Bartholomeeusen *et al*., 2012; Li *et al.*, 2013). Bartholomeeusen *et al.* showed that addition of JQ1 resulted in a release of P-TEFb from the 7SK complex, resulting in HIV-1 transcriptional elongation. Melanie Ott's lab has indicated that a BRD4 variant, BRD4S, may directly inhibit HIV-1 expression by associating with the nucleosome remodeling complex SWI/SNF (Conrad *et al.*, 2017), providing further evidence that JQ1's regulation of HIV-1 transcription is due to its ability to bind BRD4. However, it should be noted that the effects of JQ1 have so far been limited to *in vitro* analysis, and there are serious concerns regarding toxicity of several of the compounds listed here, particularly PKC agonists. In spite of promising data using cell lines, no LRA has successfully led to substantial clearance of the latent reservoir in a patient as measured by PCR.

Establishment of Latent HIV-1 and the Role of T Cell Signaling

While the concentration of Tat (Donahue *et al.*, 2012; Razooky *et al.*, 2015) and the chromatin accessibility within an infected cell are understood as critical to productive transcription and infection (Miller-Jensen *et al.*, 2012), the availability of host factors, proteins that regulate RNAPII, and transcriptional mechanisms are not fully appreciated. It is known that T cell activation is needed for both the activation of host factors

necessary for HIV-1 transcription (Acuto and Michel, 2003; Huang and Wange, 2004) as well as efficient viral integration. Therefore, T cell activation appears to be required for productive infection (Stevenson *et al.*, 1990; Oswald-Richter *et al.*, 2004). Indeed, signals from the TCR/CD3 complex and coreceptor CD28 substantially upregulate HIV-1 expression (Gruters *et al.*, 1991; Natarajan, August and Henderson, 2010). The HIV-1 protein Nef may co-opt this mechanism by amplifying TCR signaling (Fenard *et al.*, 2005; Neri *et al.*, 2011).

TCR signaling occurs through engagement of a T cell with its cognate antigen presented in the context of MHC Class I or II from the same genetic background (Dembić *et al.*, 1986; von Boehmer and Kisielow, 1990). CD4+ T cells require presentation from a Class II molecule, which are found on professional APCs (Wang and Reinherz, 2002). This engagement results in clustering of the TCR/CD3 complexes and CD28 proteins (Ohnishi *et al.*, 1995; Lillemeier *et al.*, 2010). When brought into proximity with one another, associated Src kinases, including Lck, phosphorylate both the critical Immunoreceptor Tyrosine-Based Activation Motifs or ITAMs contained within the CD3 protein as well as tyrosine residues within the cytoplasmic tail of CD28 (Gibson et al., 1996; Rossy *et al.*, 2013). These phosphorylated residues then act as binding sites for the Syk-kinase, Zap70. In turn, Zap70 is phosphorylated and becomes a key component within a newly assembled network of proteins, such as LAT and the SH2-domain containing kinases (Neumeister *et al.*, 1995; Lo *et al.*, 2018). A proximal signaling complex is orchestrated around LAT (Figure 1.4), resulting in downstream actin rearrangements (Bunnell *et al.*, 2001). In addition, the SH2-containing enzyme PLCγ1 is

recruited to the plasma membrane, where it cleaves PtdIns(4,5)P_2 (Rhee, 2001). As a result, multiple arms of the T cell receptor pathway are engaged, resulting in calcium release (Bilal *et al.*, 2015), MAP Kinase signaling (Frearson and Alexander, 1998), and NF-κB activation downstream of Protein Kinase C (PKC) (Zhao *et al.*, 2014). Activation of these multiple cascades increases transcription for a number of host genes and differentiation-determining factors (Smith-Garvin, Koretzky and Jordan, 2009; Adair *et al.*, 2016).

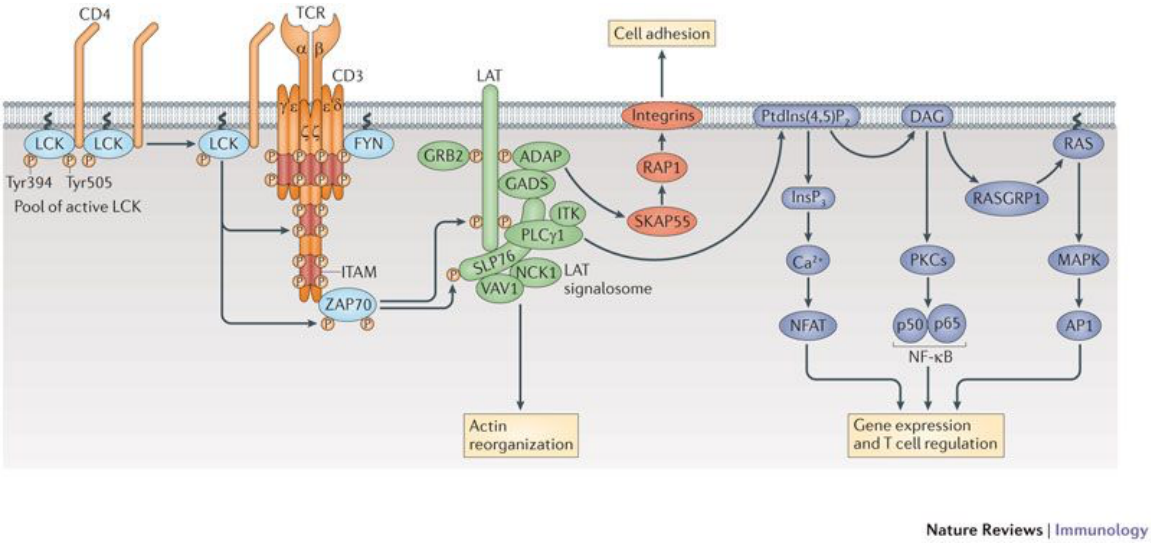

Figure 1.4: T cell receptor signaling results in activation of multiple pathways. TCR signaling leads to phosphorylation of critical tyrosine residues within ITAMs that enable the formation of a proximal signaling complex. Creation of this complex results in actin reorganization and stimulation of transcription factors downstream of PtdIns(4,5)P_2. Recreated here with permission, in its entirety from (Brownlie and Zamoyska, 2013). Figure caption is the original work of the author of this dissertation.

In addition to roles upstream of gene transcription, T cell signaling impacts cell maturation (Brocker, 1997; Pepper and Jenkins, 2011). Naïve T cells which become activated by stimulation through their cognate antigen transition into either effector populations or memory cells. Latently infected cells isolated from patients on ART

predominately express memory phenotypes (Brenchley *et al.*, 2004; Chomont *et al.*, 2009). The Planelles model of HIV-1 latency attempts to recapitulate this by differentiating CD4+ T cells into central memory cells (Bosque and Planelles, 2009).

Several papers, including those from the Henderson lab, have implicated T cell signaling in the regulation of productive HIV-1 replication (Natarajan, August and Henderson, 2010; Schiralli Lester *et al.*, 2013). For example, studies have suggested that different antigen-presenting cell subsets alter HIV-1 replication by differentially activating T cells (Kumar *et al.*, 2015). Furthermore, it has been shown that cells with low levels of activated NF- κB and decreased expression of activation markers may be biased towards harboring latent infections (Duverger *et al.*, 2009; Dahabieh *et al.*, 2014; Chavez, Calvanese and Verdin, 2015). Signals that predispose cells towards an anergic phenotype have also been linked to repression of HIV-1 (Seu *et al.*, 2015). However, these experiments fail to describe the actual signaling cascades that account for this correlation, and direct evidence is still needed that minimal TCR signaling during infection predisposes HIV-1 towards latency.

Understanding the establishment of latent HIV-1 is also essential since it has been shown that there are wide differences between the capacities to reactivate latent reservoirs from different patients. It was originally assumed that the majority of non-inducible proviruses were defective, most likely due to errors with reverse transcription. However, the Siliciano lab demonstrated that a portion of the non-inducible DNA reservoir is fully competent based on sequencing analysis, which is shown in Figure 1.5 (Ho *et al.*, 2013; Hosmane *et al.*, 2017). Our lack of knowledge regarding the exact

mechanisms which account for these various sub-populations of latently infected cells, some of which are refractory to the strongest LRAs identified so far, highlights the importance of understanding the role of the cellular environment at the time of infection on viral fate. A primary goal of my work was to understand the signaling requirements for HIV-1 infection and whether the input of signals at the time of infection shaped the size of the inducible latent reservoir.

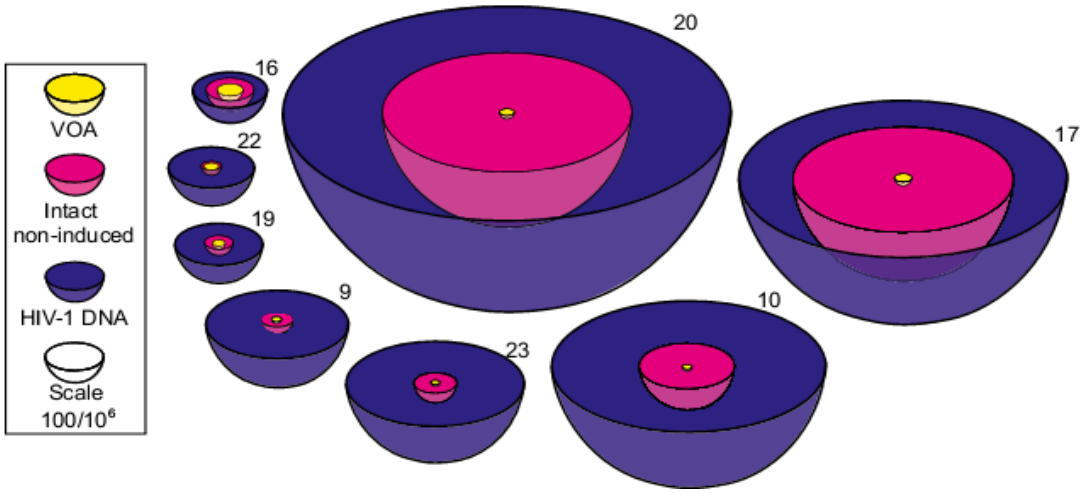

Figure 1.5: A significant portion of the latent reservoir consists of non-inducible fully competent proviruses. Depiction of the DNA reservoir from various patients on antiretroviral therapy. The size of the eggshell is an indication of the number of proviruses. The yellow sphere represents the size of the latent reservoir as measured by the viral outgrowth assay. The magenta sphere represents the size of the latent reservoir as measured by sequencing. The blue sphere represents the total DNA load. Recreated here with permission, in its entirety from (Ho *et al.*, 2013). Figure caption is the original work of the author of this dissertation.

"Block and Lock"

With the future of "shock and kill" approaches to eradication of latent HIV-1 in doubt, increasing interest has focused on the formation of the latent reservoir. If we can

determine why some cells enable productive infections while others harbor latent proviruses, perhaps we can manipulate the balance between these two populations. In fact, a growing body of research has focused on a converse strategy to "shock and kill," referred to as "block and lock." This repressive approach imagines a permanent suppressive environment for the integrated provirus, allowing a patient to cease therapy indefinitely with only periodic clinical sampling to ensure a lack of viral replication (Méndez *et al.*, 2018; Debyser *et al.*, 2018). For example, the Valente lab has focused on Tat inhibition through the preferential binding of didehydro-Cortistatin A. This prevents engagement between the TAR region and the HIV-1 transactivator (Mousseau *et al.*, 2012; Mousseau *et al.*, 2015).

The global cellular environment not only affects levels of host transcription factors but also directly alters the local chromatin landscape where the virus has integrated. If we are to achieve a "block and lock" method to repress HIV-1, we will most likely have to modify the epigenome along the provirus. This level of precise gene editing can be achieved through the use of Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR).

CRISPR associated protein 9 or Cas9 can be isolated from multiple bacterial species including *Streptococcus pyogenes* and *Staphylococcus aureus* (Cho *et al.*, 2013; Ran *et al.*, 2015). It forms an essential part of the CRISPR defense system in bacterial cells. Briefly, CRISPR works by extracting various segments of foreign DNA and inserting it into a CRISPR locus. In nature, this would often be phage DNA. When a bacterial cell is re-infected with DNA belonging to a pathogen that it has encountered

before, the complementary stored sequence will bind to the incoming DNA. This will target Cas9 to the pathogenic DNA, which will then perform its exonuclease activity to destroy the invader (Barrangou *et al.*, 2007; Mali, Esvelt and Church, 2013).

The ease which with this system works has led scientists to substitute complementary sequences to phage DNA with a guide RNA directed against a target gene of choice. In combination with the bacterial exonuclease, gene editing can then be achieved with minimal off-target effects (Kim *et al.*, 2015). A number of labs have shown promising results using CRISPR to excise HIV-1 DNA; however, it is expected that use of CRISPR in vivo will result in viral escape (Wang G *et al.*, 2016; Wang Z *et al.*, 2016). In addition, although CRISPR has relatively few off-target effects, any non-specific gene editing is a serious concern for therapeutic applications (Fu *et al.*, 2013). To prevent this occurrence, I propose using a disabled or nuclease-deficient Cas9 system (dCas9) to target chromatin repressors to HIV-1 DNA instead of an exonuclease.

Nuclease-deficient Cas9 was developed in an attempt to isolate the residues responsible for the exonuclease activity inherent to CRISPR. In order to cut both strands of DNA, Cas9 uses two separate domains, referred to as HNH and RuvC. Mutations in both domains render the Cas9 defective (Jinek *et al.*, 2012). However, dCas9 retains the targeting capabilities of CRISPR and can be used to bring transcription factors directly to a gene of interest (Zhang *et al.*, 2015). There are also attempts to modify dCas9 as an inducible system under the control of a stimulus such as rapamycin (Zetche, Volz and Zhang, 2015; Brocken, Tark-Dame and Dame, 2018).

Other labs have shown the potential for the CRISPR system to induce HIV-1 expression by fusing a nuclease-deficient Cas9 to various transcriptional activators (Zhang *et al.*, 2015; Saayman *et al.*, 2016). I propose the fusing of Cas9 to a Krüppel Associated Box (KRAB) Domain. KRAB domains are known to engage with cellular KRAB-Associated Protein-1 or Kap1 (also known as Trim28), which recruits various transcriptional repressors, resulting in gene silencing and spreading repressive chromatin marks (Friedman *et al.*, 1996; Groner *et al.*, 2010). These repressors are believed to include histone methyltransferases, histone deacetylases, and heterochromatin protein 1 (Groner *et al.*, 2010). KRAB-Kap1 has been identified as a key regulator of endogenous retroviral elements (Rowe *et al.*, 2010) and thus is a good candidate for both repressing HIV-1 and potentially mediating long-term epigenetic silencing of the provirus.

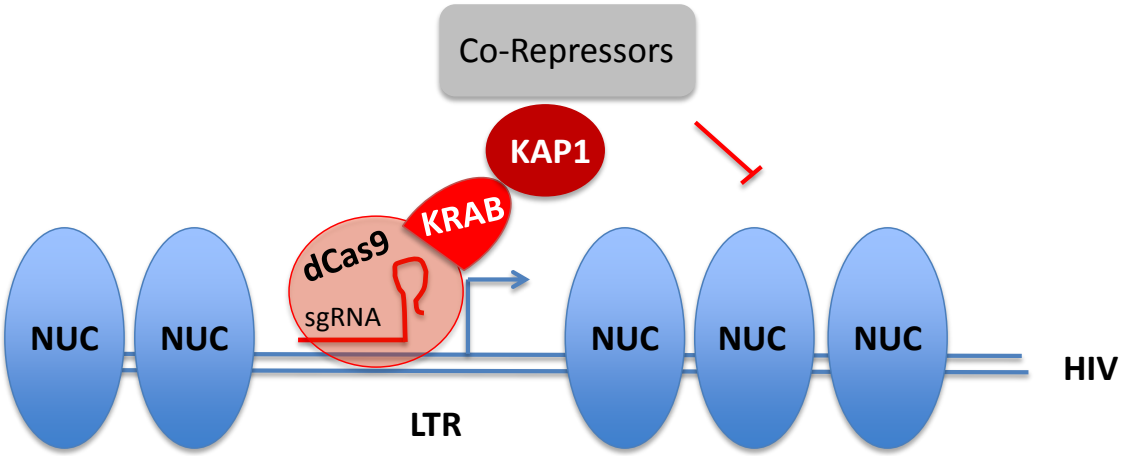

Illustration 1.1: dCas9-targeted repression of HIV-1. Nuclease-deficient Cas9 fused to a KRAB domain can be used to recruit cellular factors such as Kap1 to the integrated HIV-1 provirus in order to induce latency and remodel the local chromatin organization into a heterochromative state.

Specific Aims and Hypothesis

Significant progress has been achieved in the treatment of Human Immunodeficiency Virus. Antiretroviral therapies limit progression to AIDS through a combination of inhibitors. However, ART does not cure HIV-1 infection. If therapy is interrupted, patients experience a viral rebound due to the persistence of an inducible reservoir primarily consisting of latently infected CD4+ T cells. This forces patients to remain on ART indefinitely, but these medications have substantial side effects and do not prevent all pathologies associated with HIV-1. For these reasons, the scientific community has prioritized the search for a cure that will eliminate latent HIV-1, but more insights are needed regarding the establishment of the latent reservoir. In this dissertation, I both investigate the global cellular signals that lead to formation of latent infections and bias an infection towards latency by manipulating the local chromatin environment of the provirus.

Analysis of latently infected cells revealed that the HIV-1 long terminal repeat is associated with repressive transcription factors (Bernhard *et al.*, 2013). These repressors recruit histone deacetylases that modify the first nucleosome downstream of the transcriptional start site into a closed conformation (Williams *et al.*, 2006). As a result, RNAPII pauses prematurely and complete viral transcripts are not produced (Feinberg, Baltimore and Frankel, 1991; Zhang, Klatt, Gilmour and Henderson, 2007; Natarajan *et al.*, 2013). The host immune system then fails to recognize this latent reservoir. While data indicates a role for both integration site (Miller-Jensen *et al.*, 2012; Lelak *et al.*,

2015) and abundance of the HIV-1 transcriptional transactivator Tat in the establishment and maintenance of latency (Donahue *et al.*, 2012; Razooky *et al.*, 2015), recent work suggests that the level of cellular activation at the time of infection is also a key determinant (Duverger *et al.*, 2009; Dahabieh *et al.*, 2014; Chavez, Calvanese and Verdin, 2015). However, these studies have been correlative and direct evidence is still needed. To identify signaling cascades that participate in the establishment of HIV-1 latency, I have designed a tunable and regulated cell model that allows me to modulate T cell receptor signaling at the time of infection. Based on the evidence that increased cellular stimulation results in enhanced HIV-1 replication (Duverger *et al.*, 2009; Dahabieh *et al.*, 2014), I hypothesized that the global cellular environment at the time of HIV-1 infection determines the potential for inducible latent infection and that this axis can by bypassed by modification of the local chromatin environment. Accordingly, I addressed the following aims:

Specific Aim 1: Determine the effect of distinct T cell receptor signal strengths at the time of HIV-1 infection on viral expression within primary cells and reactivation of latent proviruses. I used a novel primary cell system to manipulate TCR signaling at the time of infection and examine the signaling requirements for efficient HIV-1 expression. To mimic TCR signaling, I transduced CD4+ T cells with chimeric antigen receptors that contain both the intracellular signaling domains of CD3ζ and CD28 along with one of several extracellular Her2 binding domains with different affinities for Her2. I used flow cytometry to confirm CAR expression, *Alu*-PCR to determine HIV-1 integration, and both RT-PCR and luciferase analysis to measure HIV-1 transcription.

With this system, I verified my hypothesis that increased T cell signaling enhances HIV-1 transcription. I also infected primary T cells and stimulated them through either the low or high affinity CAR. I then restimulated sorted non-HIV expressing cells with latency-reversing agents to measure reactivation. These experiments revealed that differential signaling at the time of infection resulted in the formation of subsets of latently infected cells with varying capacities for proviral induction.

Specific Aim 2: Analyze transcriptional landscape of the provirus among cells receiving differential stimulation at the time of HIV-1 infection. I hypothesized that cells with minimal stimulation at the time of infection display a bias for the presence of host repressors and a lack of polymerase processivity. To test this, I used chromatin immunoprecipitation to examine RNAPII processivity and the recruitment of host regulators to the transcriptional start site. I also analyzed markers of chromatin accessibility such as histone acetylation. These studies identified downstream targets of TCR-associated signals that repress HIV-1 during acute infection.

Specific Aim 3: Use a nuclease-deficient Cas9 construct to recruit host repressors to the provirus and suppress HIV-1 expression. To determine if an infection can be biased towards latency after HIV-1 integration I used a nuclease-deficient Cas9 fused to a Krüppel associated box domain in order to recruit the repressor Kap1 to the provirus. HEK293T cells were infected with single-round HIV-Luciferase and transfected with a dCas9-KRAB construct. One day later, infected cells were transfected with HIV-1 specific guide RNAs to repress viral transcription. HIV-1 expression was measured by luciferase analysis. I also electroporated latently infected

Jurkat cells with the nuclease-deficient Cas9 and HIV-specific guide RNAs to block latency reactivation as measured by RT-PCR. I verified my hypothesis that transfection with dCas9-KRAB represses HIV-1 RNA and protein expression.

My findings elucidated how TCR signaling regulates HIV-1 transcription and latency. These experiments may inform both why such a large portion of the latent reservoir is non-reactivatable as well as the efficacy of block and lock strategies, whether there are new druggable targets that can bias an infection towards or away from latency.

CHAPTER TWO: MATERIALS AND METHODS

Parts of this chapter were originally published in: Gagne M, Michaels D, Schiralli Lester G, Wong W, Gummuluru S, Henderson AJ. Strength of T Cell Signaling Regulates HIV-1 Replication and Establishment of Latency. *bioRxiv*. https://doi.org/10.1101/432401.

Cells

Jurkat CD4+ T cells (E6-1) and human embryonic kidney 293T (HEK293T) cells were obtained from American Type Culture Collection (ATCC). Jurkat cells were cultured in RPMI 1640, 5% FBS (Corning, Inc.), 100 $^{units}/_{mL}$ penicillin (Invitrogen), 100 $^{\mu g}/_{mL}$ streptomycin (Invitrogen), and 2mM L-glutamine (Invitrogen). HEK293T cells were cultured in Dulbecco's Modified Eagle Medium, 10% FBS, 100 $^{units}/_{mL}$ penicillin, 100 $^{\mu g}/_{mL}$ streptomycin, and 2mM L-glutamine. Cells were grown at 37° C with 5% CO_2.

Primary CD4+ T cells were derived from de-identified healthy blood leukapheresis packs purchased from NY Biologic. Mononuclear cells were enriched from leukopacks by centrifugation through Histopaque gradient (Sigma-Aldrich). CD4+ T cells were isolated by negative selection using EasySep Human CD4+ T Cell Enrichment Kits from StemCell Technologies. CD4+ cells were maintained in RPMI 1640, 10% FBS, 100 $^{units}/_{mL}$ penicillin, 100 $^{\mu g}/_{mL}$ streptomycin, and 2mM L-glutamine at 37° C with 5% CO_2. Prior to transduction with CARs, primary cells were supplemented with 10 $^{units}/_{mL}$ IL-2 and 10 $^{ng}/_{mL}$ IL-7. Following transduction, IL-2 was removed from most culture conditions.

J-Lat cells (6.3) were obtained from NIH AIDS Reagent Program and were cultured in RPMI 1640, 10% FBS, 100 $^{units}/_{mL}$ penicillin, 100 $^{\mu g}/_{mL}$ streptomycin, and 2mM L-glutamine. Cells were grown at 37° C with 5% CO_2. Following transduction with dCas9, J-Lat cells were cultured with 10 $^{\mu g}/_{mL}$ Blasticidin as a selection marker. Blasticidin was removed from media 2 days prior to electroporation. All cells and cell lines were split every 2-3 days.

sgRNA Screen

dsaCas9 sgRNAs were designed using the online program Benchling (Benchling, 2019) by searching the NL4-3 sequence for 23-base pair long binding sites that contained the required PAM sequence of 5'-(N)NGRRT-3'. All chosen sites (see Table 2.1) had an efficiency score of > 50% and a specificity score of > 75%. dsaCas9 sgRNAs were expressed under the control of a SFFV promoter and were fused to the required tracrRNA sequence within the lentiviral vector pHR. In addition, blank dsaCas9 sgRNAs were obtained that contained only the tracrRNA component. All dsaCas9 sgRNA plasmids were constructed in the Wilson Wong laboratory at the BU School of Biomedical Engineering.

dspCas9 sgRNAs were chosen based on a literature search (see Table 2.1), with sg361 modified from "sg362F T" (in Saayman *et al.*, 2016) in order to not exceed the required 20 base pairs for dspCas9. sg397 was obtained from "Protospacer D" in Hu *et al.*, 2014. Both sequences were purchased from IDT as Alt-R CRISPR-Cas9 crRNAs and

fused to the required sequence (GUUUUAGAGCUAUGCU) necessary to bind to the Alt-R CRISPR-Cas9 tracrRNA. Annealing of the two strands of RNA occurred as follows: 1 µL of 100 µM crRNA and 1 µL of 100 µM tracrRNA were mixed in 98 µL Nuclease-Free Duplex Buffer (IDT) at 95°C for 5 m. Annealed solutions were stored at -20°C. In addition, Scramble sgRNAs were obtained from IDT that bound to no known region of the human genome (Alt-R CRISPR-Cas9 Negative Control crRNA #1, 1072544).

crRNA Sequences		
sgRNA	sgRNA format	Sequence
dsa397	Plasmid DNA	5'- GGTGTGGCCTGGGCGGGACTG - 3′
dsa518	Plasmid DNA	5'- AGCTTTATTGAGGCTTAAGCA - 3′
dsa705	Plasmid DNA	5'- TGCCGTGCGCGCTTCAGCAAG - 3′
dsa818	Plasmid DNA	5'- GAGCGTCAGTATTAAGCGGGG - 3′
dsa2285	Plasmid DNA	5'- CCCCCTATCTTTACTTTGACG - 3′
dsa2839	Plasmid DNA	5'- AATTAGGAATACCACATCCCG - 3′
dsa5876	Plasmid DNA	5'- AAGCAGTTTTAGGCTGACTTC - 3′
dsp361	RNA	5'- CUACAAGGGACUUUCCGCUG - 3′
dsp397	RNA	5'- GUGUGGCCUGGGCGGGACUG - 3′

Table 2.1: Sequences used for crRNA screen. dsaCas9 sgRNAs and dspCas9 sgRNA sequences are listed.

Viruses, Transfections, and Transductions

CARs were driven by a SFFV promoter in the lentiviral vector pHR (Schier *et al.*, 1996; Chmielewski *et al.*, 2004). pNL4-3.Luc.R-E- was obtained from NIH AIDS Reagent Program. BRU-ΔEnv-GFP was a gift from Dr. Gregory Viglianti (Boston University). CAR lentiviruses were made by transfection of lentiviral expression vectors, VSV-G env, Rev, Tat, and Gag-Pol constructs into HEK293T cells with 45μL polyethylenimine (1 $^{mg}/_{mL}$) per 6x10^6 cells. Transfections of HIV-1 included only viral plasmids and envelope plasmids. Supernatants of lentiviruses were collected, filtered with 0.45μm syringe filter (Corning), concentrated by centrifuging through a 20% sucrose gradient, and titered on CEM cells (Janas and Wu, 2009). I used a range of multiplicity of infections, but most viruses and lentiviruses within this paper were concentrated to approximately 1x10^6 $^{IU}/_{mL}$.

Transfections of dCas9-KRAB in Chapter Four for the purposes of making lentiviral vectors were performed similarly. Cotransfections of pNL4-3.Luc.R-E-, dCas9-KRAB, and sgRNAs into HEK293T cells were also performed similarly but without any additional accessory or structural gene plasmids.

For transductions with CAR vectors, primary cells were stimulated for 5-6 h with 10 $^{\mu g}/_{mL}$ PHA, washed in PBS, and spinoculated by spinning cells with lentivirus and 5 $^{\mu g}/_{mL}$ polybrene (Millipore) at 1200g for 90 min. Cells were then supplemented with fresh RPMI and IL-7, cultured overnight, and washed in PBS 18 h later. Cells were rested for

one week to return to a resting state as confirmed by low CD69 expression prior to HIV-1 infection.

Transductions of Jurkat cells with CAR vectors and J-Lat cells with dCas9 vectors were performed similarly. However, no PHA stimulation or cytokine treatment was required. CAR-expressing Jurkat cells were sorted based on mCherry expression and cultured as pure populations. For sorting details, see Flow Cytometry Methods below.

CAR Stimulation and Infections

Non-tissue culture treated plates were coated overnight at 37°C with 1 $^{\mu g}/_{mL}$ Her2 (Recombinant Human ErbB2/Her2 Fc Chimera Protein from R&D Systems, 1129-ER). Her2 solution was removed from wells, plates were washed 3 times in PBS, and wells were blocked for 1 h with a 5% FBS-PBS solution.

CAR+ Jurkat or primary CD4+ T cells were infected with HIV-1 and simultaneously plated in Her2-treated wells. For experiments in which latently infected cells were generated, cells were spinoculated in the Her2-treated wells at 1200xg for 90 min and then supplemented with fresh RPMI and IL-7. Following overnight infection, cells were washed and either lysed or maintained in fresh media in the absence of Her2.

For some experiments, CAR-expressing cells were treated with 10 μM PP2 or PP3 (Calbiochem - Millipore Sigma), Src kinase inhibitor and pharmacologically inactive analog respectively, at the time of HIV-1 infection.

Infections of HEK293T cells with HIV-1 were performed 24 h prior to dCas9-KRAB and sgRNA transfection.

Electroporations

For electroporations, $1x10^6$ J-Lat cells were centrifuged for 10 min at 90xg. Cells were then resuspended in 90 μL 1SM buffer. 1SM buffer (5mM KCl, 15mM $MgCl_2$, 120mM Na_2HPO_4 pH 7.2, 25mM sodium succinate, 25mM manitol) was prepared as described in (Chicaybam *et al.*, 2013). Cells were incubated with 10 μL sgRNA (1000 nM) in cuvettes. Electroporation was performed in Amaxa Biosystems Nucleofactor I with program setting X-005. After electroporation, cells were cultured in RPMI 1640, 20% FBS (Corning, Inc.), 100 $^{units}/_{mL}$ penicillin (Invitrogen), 100 $^{\mu g}/_{mL}$ streptomycin (Invitrogen), and 2mM L-glutamine (Invitrogen) at 37° C with 5% CO_2. 24 h later, cells were washed in PBS and replated in normal culture media as described above.

Latency Reversal

For reactivation of latent CAR-expressing primary cells, mCherry (CAR) positive and GFP (HIV-1) negative cells were sorted at 6 or 7 days post HIV-1 infection. Cells were cultured with the following concentrations of LRAs: 5 $^{ng}/_{mL}$ PMA and either 10 or 100uM ionomycin for 2.5 h, Dynabeads human T-activator CD3/CD28 beads at a ratio to cells of 1:1 for 24 h, 50 μM SBHA for 24 h, and 25nM Bryostatin for 24 h. Cells

reactivated with PMA were washed in PBS and re-plated in media. All reactivated cells were incubated with 10 $^{ng}/_{mL}$ IL-7. Cells were cultured overnight prior to fixation for flow analysis.

J-Lat cells were treated with 10 ng/mL TNF-α in order to induce latency reversal. Stimulation took place five days following electroporation. RNA was isolated for qRT-PCR 24 h post latency reversal.

Luciferase Analysis

Jurkat cells were washed and lysed for luciferase analysis 24 h post infection, while primary T cells were measured at 4 days post infection. HEK293T cells were washed and lysed for luciferase analysis 48 h post sgRNA and dCas9-KRAB transfection. Luciferin (Promega) was added and luciferase activity was measured via BioTek Synergy HT Microplate Reader.

Flow Cytometry

Flow data were collected on an LSRII from BD Biosciences. Zombie UV Fixable Viability Kit (BioLegend) was used as live/dead stain for reactivation experiments. All cells were washed and fixed in a final concentration of 2% paraformaldehyde prior to analysis. Cell sorting was performed on a MoFlo Astrios from Beckman Coulter. All flow experiments performed at Boston University School of Medicine Flow Cytometry Core Facility.

CAR stimulation was determined by CD69 expression (Brilliant Violet 421 anti-human CD69 antibody; Clone FN50, BioLegend).

Memory cell phenotypes were characterized based upon CCR7 and CD45RA expression (Pe/Cy7 anti-human CCR7 antibody; Clone G043H7, BioLegend and PerCP/Cy5.5 anti-human CD45RA antibody; Clone HI100, BioLegend).

Microarray Analysis and Heatmap Formulation

Primary CD4+ T cells were transduced with chimeric antigen receptors and allowed to return to a resting state for 1 week. Cells were then stimulated overnight with plate-bound Her2 as described above. Untransduced CD4+ T cells were left unstimulated or were plated in a solution of 1 $^{\mu g}/_{mL}$ CD28 (Mouse Anti-Human CD28, #555725, BD Biosciences) on previously coated wells of 1 $^{\mu g}/_{mL}$ CD3 (Mouse Anti-Human CD3, #555329, BD Biosciences). Cells were then washed in PBS and lysed for RNA extraction using Qiagen miRNeasy Mini Kit (#217004). RNA was stored at -80°C until delivery to the BU Microarray and Sequence Resource Core Facility. At the Microarray core, cDNA was made and samples were run on a Human Clariom S Array. The Microarray core also provide the statistical support described here.

Human Clariom S CEL files were normalized to unstimulated cells to produce gene-level expression values using the implementation of the Robust Multiarray Average (RMA) (Irizarry *et al.*, 2003) in the *affy* package (version 1.36.1) (Gautier *et al.*, 2004) including in the Bioconductor software suite (version 2.11) (Gentleman *et al.*, 2004) and

an Entrez Gene – specific probeset mapping (21.0.0) from the Molecular and Behavioral Neuroscience Institute (Brainarray) at the University of Michigan (Dai *et al.*, 2005, University of Michigan, 2019). Array quality was assessed by computing Relative Log Expression (RLE) and Normalized Unscaled Error (NUSE) using the *affyPLM* package (version 1.34.0). Analyses of variance were performed using the *f.pvalue* function in the *sva* package (version 3.4.0). Differential expression was assessed by performing Student's *t* test on the coefficients of linear models created using the *lmFit* function in the *limma* package (version 3.14.4). In this way, a one-way ANOVA *p* value was obtained using a linear mixed effects modeling approach to account for differences between donors.

Correction for multiple hypothesis testing was accomplished using the Benjamini-Hochberg false discovery rate (FDR) (Benjamini and Hochberg, 1995). All microarray analyses were performed using the R environment for statistical computing (version 2.15.1). All genes with FDR *q* values below 0.01 were plotted on a heatmap and arbitrarily separated into 5 clusters based on expression profiles.

Principal Component Analysis (PCA) was performed using the *prcomp* R function with expression values that had been normalized across all samples to a mean of zero and a standard deviation of one. The separation of samples by treatment group along the PC1 axis explains 29% of all variance in the experiment.

Measurement of HIV-1 Provirus Using Nested *Alu*-PCR

For measuring integrated HIV-1 provirus, a nested PCR strategy was adapted from (Agosto *et al.*, 2007). Briefly, integrated HIV-1 DNA was amplified using forward primers for the luciferase sequence and reverse primers for human *Alu* (see Table 2.2). The first reaction was performed on a TProfessional Thermocycler from Biometra according to the following conditions: 4 m at 95° followed by 20 cycles of 15 s at 93°, 15 s at 50°, and 2.5 m at 70°. A second round of amplification was then performed using a forward primer, a reverse primer, and a probe for real time PCR within the HIV-1 3' R / U5 region (see Table 2.2). The amount of amplified copies of HIV-1 was determined based on an NL4-3 plasmid copy standard. The second reaction was performed on an Applied Biosystems QuantStudio 3 Real-Time PCR system with heating for 4 m at 95° and real-time PCR conditions of denaturation for 15 s at 95°, annealing for 30 s at 60°, and extension for 1 m at 72°.

Oligos Used for *Alu*-PCR			
Reaction	Gene / Target	Primer Direction	Primer Sequence
1st Step	*Alu*	Forward	5'-CGTCGCCAGTCAAGTAAC-3′
	luc	Reverse	5'-CTGTAATCCCAGCAGTTTGGGAGGC-3′
2nd Step	3' R/U5	Forward	5′-GCCTCAATAAAGCTTGCCTTGA-3′
		Reverse	5′-TCCACACTGACTAAAAGGGTCTGA-3′
		Probe	5′-FAM-CCAGAGTCACACAACAGACG-TAMRA-3′

Table 2.2: Oligos used for *Alu*-PCR. Oligos are listed for each reaction step.

Measurement of HIV-1 mRNA by RT-PCR

RT-PCR for Chapter Three

RT-PCR for HIV-1 mRNA spliced variants was performed using forward primers and reverse primers for spliced HIV-1 *env* and *tat* sequences. RT-PCR for HIV-1 mRNA after latency reversal was performed using forward primers and reverse primers for unspliced HIV-1 *tat* sequence. All values for both assays were normalized against beta-actin as a housekeeping gene (see Table 2.3). The reaction was performed on an Applied Biosystems QuantStudio 3 Real-Time PCR system with heating for 15 m at 94° and real-time PCR conditions of denaturation for 15 s at 94°, annealing for 30 s at 60°, and

extension for 30 s at 72°. Relative levels of HIV-1 mRNA were determined by delta-delta CT.

Oligos Used for RT-PCR in Chapter Three		
Gene / Target	Primer Direction	Primer Sequence
env (spliced)	Forward	5'-TCCCTCAGACCCTTTTAGTCAG-3'
	Reverse	5'-GATTACTATGGACCACACAACTATTG-3'
tat (spliced)	Forward	5'-TCCCTCAGACCCTTTTAGTCAG-3'
	Reverse	5'-CATCTGTCCTCTGTCAGTTTC-3'
tat (unspliced)	Forward	5'-GGAGCCAGTAGATCCTAGAC-3′
	Reverse	5'-CTTGGCAATGAAAGCAACAC-3′
ACTB	Forward	5'-TGGGACGACATGGAGAA-3′
	Reverse	5′-GGGTGTTGAAGGTCTCAAA-3'

Table 2.3: Oligos used for RT-PCR in Chapter Three. Oligos are listed for each gene of interest or spliced transcript.

RT-PCR for Chapter Four

RT-PCR for HIV-1 mRNA after latency reversal was performed using forward primers and reverse primers for unspliced HIV-1 *gag* sequence, and all values were normalized against beta-globin as a housekeeping gene (see Table 2.4). The reaction was performed on an Applied Biosystems QuantStudio 3 Real-Time PCR system with heating

for 15 m at 94° and real-time PCR conditions of denaturation for 15 s at 94°, annealing for 30 s at 60°, and extension for 30 s at 72°. Primers for HIV-1 were based on Malnati *et al.*, 2008. Relative levels of HIV-1 mRNA were determined by delta-delta CT.

Oligos Used for RT-PCR in Chapter Four		
Gene / Target	Primer Direction	Primer Sequence
gag	Forward	5'-TACTGACGCTCTCGCACC-3′
	Probe	5'-FAM-CTCTCTCCTTCTAGCCTC-NFQMGB-3'
	Reverse	5'-TCTCGACGCAGGACTCG-3′
β-globin	Forward	5'-CCCTTGGACCCAGAGGTTCT-3'
	Probe	5'-FAM-GCGAGCATCTGTCCACTCCTG ATGCTGTTATGGGCGCTCGC-NFQMGB-3'
	Reverse	5'-CGAGCACTTTCTTGCCATGA-3'

Table 2.4: Oligos used for RT-PCR in Chapter Four. Oligos are listed for each gene of interest. HIV-1 primers span an unspliced region.

Chromatin Immunoprecipitation (ChIP)

ChIP was performed according to Natarajan *et al.*, 2013 with the addition of a nuclei isolation step using Farnham Lysis Buffer prior to sonication with a BioRupter Pico. Briefly, cells were washed in PBS and fixed in a final concentration of 1% formaldehyde in methanol. Crosslinking was quenched by addition of glycine to a final

concentration of 240mM. Cells were then washed, centrifuged, and flash frozen in liquid nitrogen. Pellet was lysed in Farnham Lysis Buffer (5mM PIPES pH 8.0, 85mM KCl, 0.5% NP-40) with addition of Halt Protease and Phosphatase Inhibitor Single-Use Cocktail from ThermoFisher before centrifugation to obtain nuclei fraction. Nuclei were lysed in RIPA buffer prior to sonication in BioRupter Pico for 15 m with alternating 30 s cycles. Samples were centrifuged to remove debris and pre-cleared with addition of 50% protein A sepharose bead for 30 m at 4°C. Beads were then pelleted and supernatants were split into 100µL portions as input DNA and multiple 300µL portions for sample analysis. Samples were incubated with antibodies overnight at 4°C. Antibody-bound proteins and cross-linked DNA were isolated by addition of 50% protein A sepharose beads for 2 h at 4°C prior to centrifugation. Immunoprecipitates were washed with low salt (0.1% SDS, 1% Triton X-100, 2mM EDTA, 20mM Tris-HCl pH 8.0, 150mM NaCl), high salt (0.1% SDS, 1% Triton X-100, 2mM EDTA, 20mM Tris-HCl pH 8.0, 500mM NaCl), lithium wash (0.25M LiCl, 1% NP-40, 1% sodium deoxycholate, 1mM EDTA, 10mM Tris-HCl), and Tris-EDTA buffers (10mM Tris, 1mM EDTA) before use of elution buffer (1% SDS, 0.1M $NaHCO_3$). Cross-linking was reversed with addition of 5M NaCl overnight at 65°C to both samples and input DNA before addition of proteinase K to isolate DNA. Sample DNA was purified using ChIP DNA Clean & Concentrator Kit (Zymo Research).

Antibodies used included anti-NELF-d (Antibody TH1L from Proteintech Group), anti-RNAPII antibody (Clone N20 from Santa Cruz Biotechnology), anti-histone

H3 antibody (Product 06-599 from Millipore Sigma), and Normal Rabbit IgG (Product 12-370 from Millipore Sigma).

Primers used for the transcriptional start site include the forward primer at +30 and the reverse primer at +239. Primers used for transcriptional elongation include the forward and reverse primers within the *tat* gene (see Table 2.5).

Oligos Used for Chromatin Immunoprecipitation Assays		
Gene / Target	Primer Direction	Primer Sequence
TSS* (+30)	Forward	5'-CTGGGAGCTCTCTGGCTAACTA-3′
TSS* (+239)	Reverse	5'-AGATCTCCTCTGGCTTTAC-3′
tat (+5379)	Forward	5'-GGAGCCAGTAGATCCTAGAC-3′
tat (+5482)	Reverse	5'-CTTGGCAATGAAAGCAACAC-3′

Table 2.5: Oligos used for chromatin immunoprecipitation. Oligos are listed for each gene region of interest. Asterisk (*) refers to HIV-1 transcriptional start site.

Statistical Analysis

All statistical analysis performed using unpaired student's *t* test except for Microarray Analysis as detailed above.

CHAPTER THREE: STRENGTH OF T CELL SIGNALING REGULATES HIV-1 REPLICATION AND ESTABLISHMENT OF LATENCY

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INTRODUCTION

Experimental Rationale

HIV-1 persists in a transcriptionally silent latent state in long-lived memory T cells. Although antiretroviral therapies suppress HIV-1 replication, interruption of treatment results in rapid viral rebound. Therefore, HIV-1 patients must remain on ART indefinitely, despite long term side effects, development of treatment resistance, and viral-induced inflammation (Wong *et al.*, 1997; Chun *et al.*, 1997; Harrigan, Whaley and Montaner, 1999). For this reason, one strategy currently being explored for cure efforts is "shock and kill," in which latent HIV-1 is reactivated in conjunction with ART using latency-reversing agents. Following reactivation, infected cells are predicted to be eliminated by HIV-specific immunity or virally induced apoptosis. However, clinical trials using LRAs have only minimally perturbed the size of the viral reservoir (Sagot-Lerolle *et al.*, 2008; Archin *et al.*, 2010; Archin *et al.*, 2012).

A cure for latent HIV-1 will require a better understanding of the biochemical factors involved. Latency in chronically infected primary cells and cell lines is regulated by multiple transcriptional mechanisms including NF-κB activation, chromatin accessibility, provirus transcription initiation, Tat availability, P-TEFb sequestration, and transcriptional elongation (Quivy, De Walque and Van Lint, 2007; Ruelas and Greene, 2013; Agosto, Gagne and Henderson, 2015; Cary, Fujinaga and Peterlin, 2016; Agosto and Henderson, 2018). However, what is not understood is how latency is initially established within a cell and if events at the time of HIV-1 infection influence the transcriptional status of the provirus. These questions are relevant since the latent reservoir is established within the first two weeks of infection (Chun *et al.*, 1998; Whitney *et al.*, 2014). New cure strategies will need to limit the size of the reservoir at early time points.

One mechanism that could predispose HIV-1 towards active replication or transcriptional repression and latency is signaling through the T cell receptor. Engagement of the TCR and costimulatory CD28 molecule result in a multitude of cellular outcomes that influence HIV-1 replication including cytoskeleton reorganization, the activation of transcription factors, enhanced RNAPII processivity, and chromatin remodeling (Huang and Wange, 2004; Kim *et al.*, 2011; Allison *et al.*, 2016). I hypothesized that the magnitude of T cell signaling during HIV-1 infection will dictate the course of the infection. In order to manipulate signal strength received by a T cell at the time of HIV-1 infection, I utilized chimeric antigen receptors (CARs) that recapitulate T cell receptor and CD28 signaling.

Chimeric Antigen Receptors

Chimeric antigen receptors or CARs are engineered ligand binding domains fused to signaling domains of interest. In this way, researchers can approximate endogenous receptor signaling but via a mechanism that they can control (Gross and Eshhar, 1992). CARs are widely used as cancer therapeutics where they can repurpose either NK cells or T cells to specifically recognize an oncogenic marker (Sommermeyer *et al.*, 2016; Romanski *et al.*, 2016). One potential target is human epidermal growth factor receptor 2. Her2 is a receptor tyrosine kinase involved in cellular activation (Lee *et al.*, 1989); its overexpression correlates with several pathologies including breast cancer (Berns *et al.*, 1992), pancreatic cancer (Yamanaka *et al.*, 1993), and glioblastomas (Ahmed *et al.*, 2010). Therefore, multiple labs have attempted to use chimeric antigen receptors specific for Her2 in order to drive CD8+ T cells towards elimination of Her2+ cells. For instance, in a Phase I clinical trial for patients with Her2-specific pancreatic cancer, at least one patient achieved a 50% reduction in the number of his lesions (Feng *et al.*, 2018).

The recognition component of the Her2 chimeric antigen receptor used in my system consists of a single-chain variable fragment (scFv). Single-chain variable fragments engineered to bind Her2 were originally developed in the 1990's. Schier *et al.* screened a scFv library and discovered the C6.5 fragment, which was later mutated to produce a number of other scFvs with differing affinities for the Her2 ligand (Schier *et al.*, 1996). This panel of Her2 receptors span 3 logs of affinity for their cognate antigen. The Wong laboratory at Boston University cloned these ligand-binding domains onto a

receptor with the intracellular signaling domains of CD3ζ and CD28, the two main components of the T cell receptor signaling complex. CD3ζ contains the six critical ITAMs (immunoreceptor tyrosine-based activation motifs) that are responsible for signal transduction due to their capacity to become phosphorylated (Bettini *et al.*, 2017). CD28 also contains multiple tyrosine residues that become phosphorylated, although they do not form a classic ITAM motif (Natarajan, August and Henderson, 2010; Ogawa *et al.*, 2013). By providing Her2 to this system, I aimed to induce similar signaling cascades to those activated by T cell receptor recognition of a MHC-peptide complex. Through these chimeric antigen receptors, which are identical apart from their Her2-binding domain, I was able to modulate the strength of signal that a cell receives. Differences in Her2 binding correlated with differential induction of T cell responses, providing our lab with a tool to manipulate cellular stimulation at the time of viral infection. A similar approach, in which various CD3ζ ITAMs were mutated to prevent phosphorylation, resulted in phenotypic and functional differences in CAR-expressing CD8+ T cells (Feucht *et al.*, 2018). This study provided supporting evidence for my hypothesis that signaling differences downstream from a TCR-based CAR could be used to interrogate the role of the TCR on HIV-1 expression.

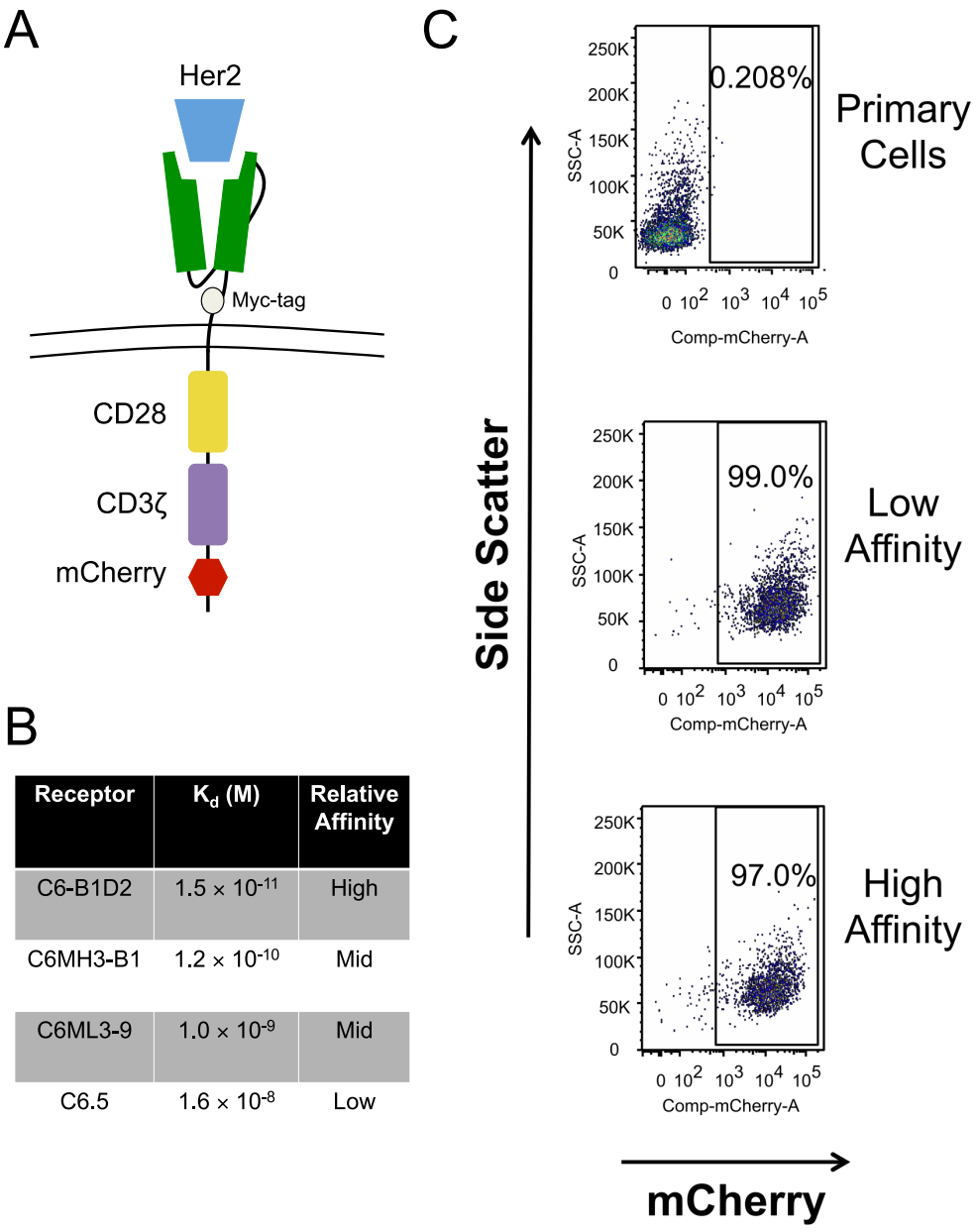
Using these CARs, I demonstrate that induction of stronger T cell receptor signaling at the time of HIV-1 infection increases subsequent HIV-1 transcription and replication. Robust signals also facilitated the formation of latently infected cells that were readily inducible upon secondary stimulation with phorbol esters, as well as PKC agonists. Minimal signaling through CARs, although sufficient for HIV-1 integration,

failed to support robust viral expression and interestingly, generated a deep-seated latent infection. Transcriptional elongation of HIV-1 provirus was limited by RNAPII pausing in the absence of CAR signaling; however, strong CAR signaling correlated with decreased Negative Elongation Factor binding and enhanced RNAPII processivity. My results suggest a model in which signaling strength influences HIV-1 transcription and establishment of latency at the time of initial infection of CD4+ T cells.

RESULTS

CARs Induce T Cell Signaling

To examine how signaling cascades downstream from the T cell receptor regulate HIV-1 transcription, I utilized CARs as can be seen in Figure 3.1A. Intracellular signaling domains for the CARs include CD3ζ with its ITAMs and the CD28 costimulatory domain with its four critical tyrosine residues (Chmielewski, Hombach and Abken, 2014). Furthermore, a mCherry tag provides a marker for positive selection of CAR+ cells. The extracellular ligand-binding domains of the CARs consist of a single chain variable fragment that recognizes receptor tyrosine-protein kinase erbB-2 (Her2) (Schier *et al.*, 1996; Chmielewski, *et al.*, 2004). By using different scFvs, a library of CARs with variable binding affinities for Her2 ligand spanning three logs was generated (Figure 3.1B). CARs were transduced into Jurkat T cells and primary CD4+ T cells. By enriching for mCherry, I obtained CAR+ populations that were >90% pure (Figure 3.1C).



Receptor	K_d (M)	Relative Affinity
C6-B1D2	1.5×10^{-11}	High
C6MH3-B1	1.2×10^{-10}	Mid
C6ML3-9	1.0×10^{-9}	Mid
C6.5	1.6×10^{-8}	Low

Figure 3.1: Chimeric antigen receptors used for tunable T cell signaling. *(A)* The design of CARs including CD3ζ and CD28 signaling domains. (*B*) CAR single chain variable fragments with their corresponding dissociation constants for the Her2 ligand. I refer to these CARs by their relative ligand affinity. (*C*) Enrichment of primary CD4+ T cells based on mCherry expression following CAR transduction. See also Figures 3.2 and 3.3.

I examined whether stimulation through the CARs lead to global transcriptional changes consistent with T cell receptor engagement. These changes would include both upregulation of activation markers and key cytokines as well as corresponding downregulation of other gene networks in order to dampen the level of immune activation. To analyze the effect of Her2 stimulation on CAR-expressing cells, I cultured low affinity and high affinity CAR-expressing primary CD4+ T cells with plate-bound Her2 ligand for 24 h as well as untransduced CD4+ T cells with or without CD3 and CD28 antibodies. I then extracted the RNA and performed microarray analysis using a Human Clariom S array. All gene expression levels were compared to the baseline of unstimulated cells, and those genes whose one-way Anova FDR-corrected *q* values were less than 0.01 were selected. This allowed for the creation of a heatmap of 4,966 significantly modified genes clustered based on their expression profiles. Clusters 4 and 5 represent genes that are downregulated upon cell activation, while Clusters 1 and 3 represent genes that are clearly upregulated upon cellular stimulation. As can be seen in Figure 3.2, stimulation through the low or high affinity CARs represents intermediate phenotypes between that of the unstimulated or TCR-engaged populations. The log2 expression of a selection of well-known genes from Clusters 1 and 3 are listed in Table 3.1. Our lab is interested in further exploring how suboptimal cellular activation leads to unique phenotypes. However, for the purposes of this paper, the pathways and genes expected to be activated downstream from the T cell receptor pathway are indeed being engaged, confirming that binding of the receptors provide me with a way to activate a range of signaling inputs at the time of infection.

	Untransduced CD4+			Low Affinity + Her2			High Affinity + Her2			Anti – CD3/CD28		
	Donor 1	Donor 2	Donor 3	Donor 1	Donor 2	Donor 3	Donor 1	Donor 2	Donor 3	Donor 1	Donor 2	Donor 3
CD69	6.6	6.7	7.2	7.9	7.9	8.0	8.3	8.3	8.2	8.3	8.2	7.8
PDCD1	5.6	5.9	5.6	6.0	6.2	6.5	6.7	6.4	6.9	6.6	7.0	7.3
CTLA4	4.5	4.6	5.4	5.8	6.1	6.0	6.3	6.5	6.4	6.9	6.9	6.8
IL2	1.7	1.5	1.3	3.5	4.3	3.7	4.8	4.9	4.9	6.9	7.8	7.3
IL21R	3.4	3.3	3.6	4.5	4.5	4.1	4.7	4.6	4.3	5.1	4.7	4.7
IRF4	7.8	7.7	7.3	8.7	9.5	9.3	9.0	9.3	9.3	9.1	9.1	9.3
IFNG	2.3	4.7	6.4	3.4	5.2	6.7	4.3	6.7	7.5	8.3	9.2	10.8
TNF	6.5	6.5	7.2	6.7	6.5	7.1	7.1	7.3	7.6	8.3	8.5	8.8
TRAF1	7.5	7.6	7.8	8.3	8.0	8.1	8.5	8.0	8.3	8.2	8.1	8.4
KLF10	6.0	7.0	6.4	7.8	7.9	7.9	8.1	8.1	8.3	8.1	8.4	8.6
JUN	4.2	4.8	5.2	5.5	5.3	6.0	5.7	5.9	6.1	5.5	6.0	6.2
FOXP3	6.9	6.4	6.9	6.6	6.6	6.7	6.6	6.5	6.4	7.7	7.0	7.3
CDK2	7.0	7.8	7.7	7.7	8.4	7.5	8.0	8.6	7.6	9.2	9.1	8.8

Table 3.1: Log2 expression of differentially regulated genes upon cell activation. A selection of commonly described genes located in Clusters 1 and 3 from the heatmap shown in Figure 3.2 are presented along with their log2 expression values. This list is in no way comprehensive and is shown as an example of the types of genes upregulated upon CAR stimulation.

Principal component analysis was also performed on the genes identified as significantly different from the unstimulated CD4+ T cell condition. This analysis, along with the full list of genes used for the creation of the heatmap in Figure 3.2 is provided in the Appendix.

Cells were also examined for the expression of phenotypic markers following stimulation. I monitored CD69, a transmembrane lectin and a marker for CD4+ T cell activation, by flow cytometry before and after receptor activation with Her 2 (Figure 3.3). Primary CD4+ T cells transduced with either the low affinity or the high affinity receptors were stimulated with plate-bound Her2 ligand for 24 h. In the absence of ligand, less than 7% of the cells were positive for CD69, verifying that there is no ectopic

CAR signaling. Activating cells with Her2 induced CD69 expression in the low affinity and high affinity receptors relative to their affinity for ligand.

I also looked at markers associated with T cell maturation. One week post stimulation, primary cells stimulated through either the low or high affinity receptor were analyzed for expression of memory markers CCR7 and CD45RA. CCR7 is a lymph node homing receptor, and CD45RA is downregulated upon memory cell differentiation. Activation through the endogenous T cell receptor using antibodies to CD3 and CD28 resulted in the expansion of the CCR7+ CD45RA- central memory population and to a lesser extent a CCR7- CD45RA- pool of effector memory cells (Figure 3.4). CAR engagement regardless of receptor affinity polarized cells towards similar memory cell phenotypes. Taken together, these data demonstrate that CARs can be used to activate a spectrum of T cell responses and provide a tool to modulate T cell signaling. Importantly, the CARs do not drive cells towards an aberrant phenotype.

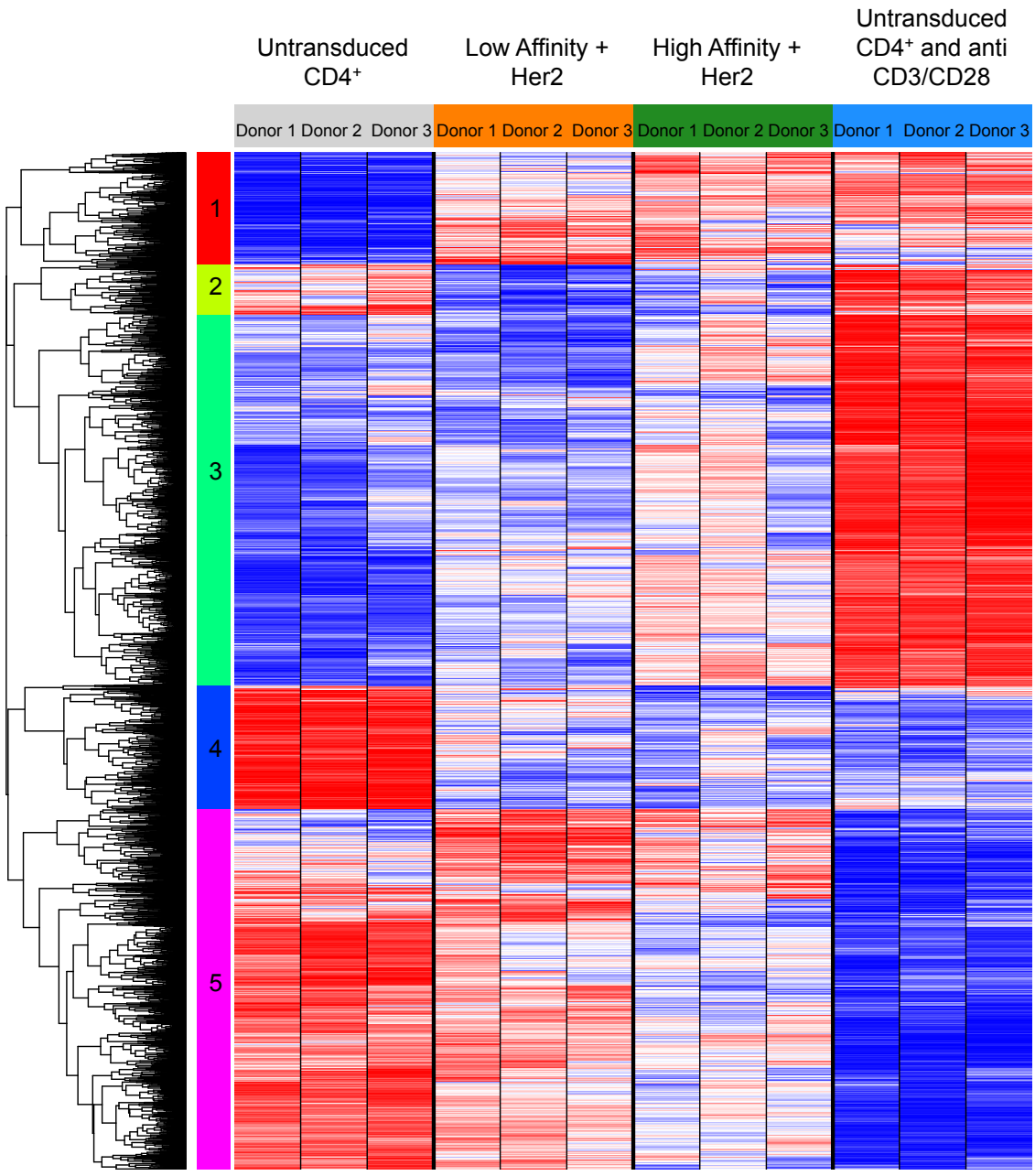


Figure 3.2: Signaling through chimeric antigen receptors alters the expression of genes downstream from the T cell receptor. CD4+ T cells isolated from healthy human donors were transduced with low affinity or high affinity CARs and then allowed to return to a resting state. Cells were either then stimulated through the receptor or left unstimulated. RNA was isolated 24 h later and converted to cDNA before being run on a Human Clariom S array. Gene expression levels for both cell types and TCR-stimulated CD4+ T cells were compared to unstimulated cells. All genes with a one-way Anova FDR-corrected q value of < 0.01 were plotted in a heatmap and clustered according to expression profiles. Data is presented as a heatmap based on RNA expression and represents three independent donors.

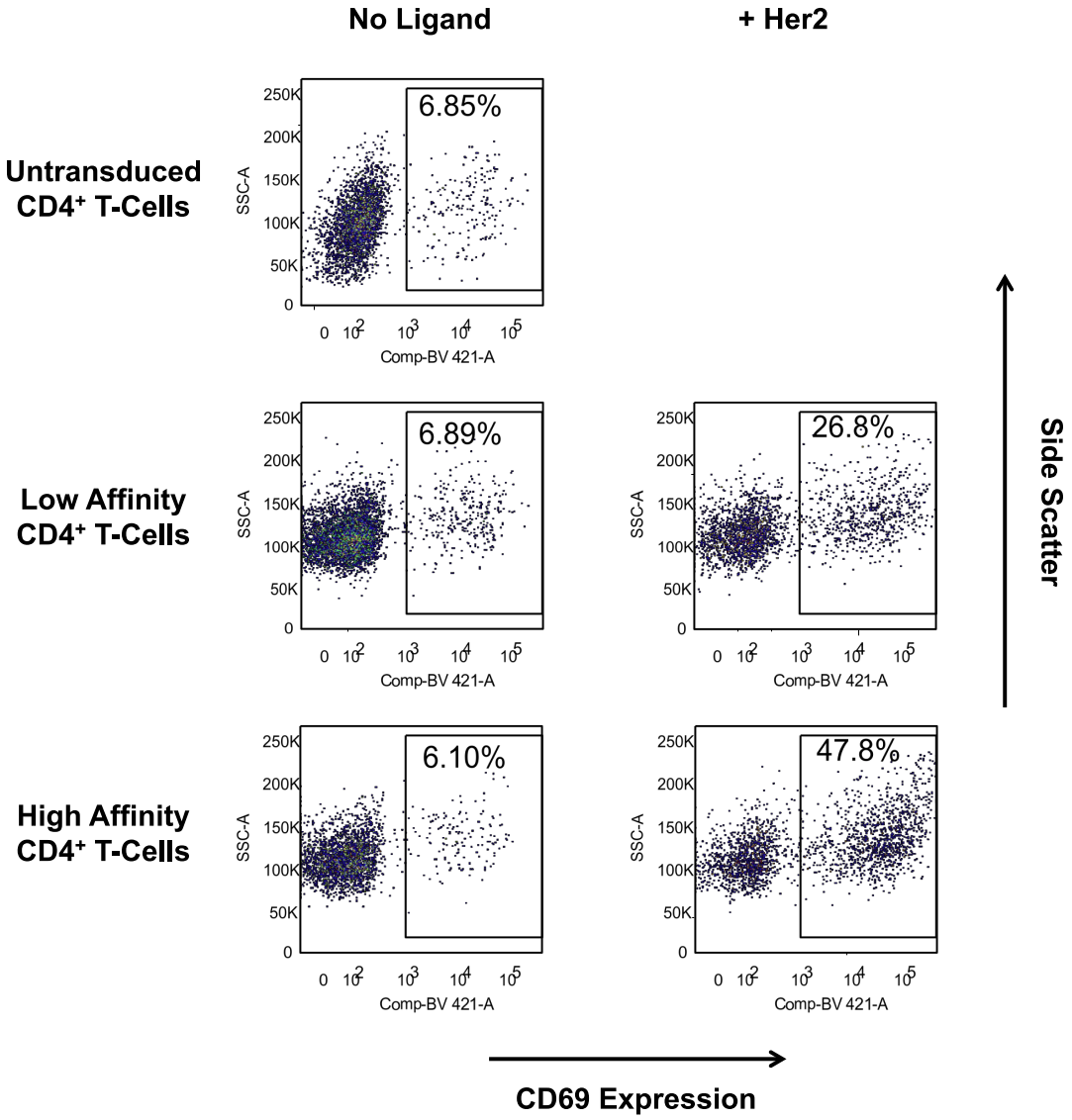


Figure 3.3: Differential signaling through chimeric antigen receptors. CD4+ T cells isolated from healthy human donors were transduced with low affinity or high affinity CARs and then allowed to return to a resting state. Cells were either then stimulated through the receptor or left unstimulated. CD69 expression was compared to a negative control of untransduced cells one day after Her2 stimulation. Data is presented as dot plots based on flow cytometry analysis and is from a representative experiment that has been performed four times with different donors.

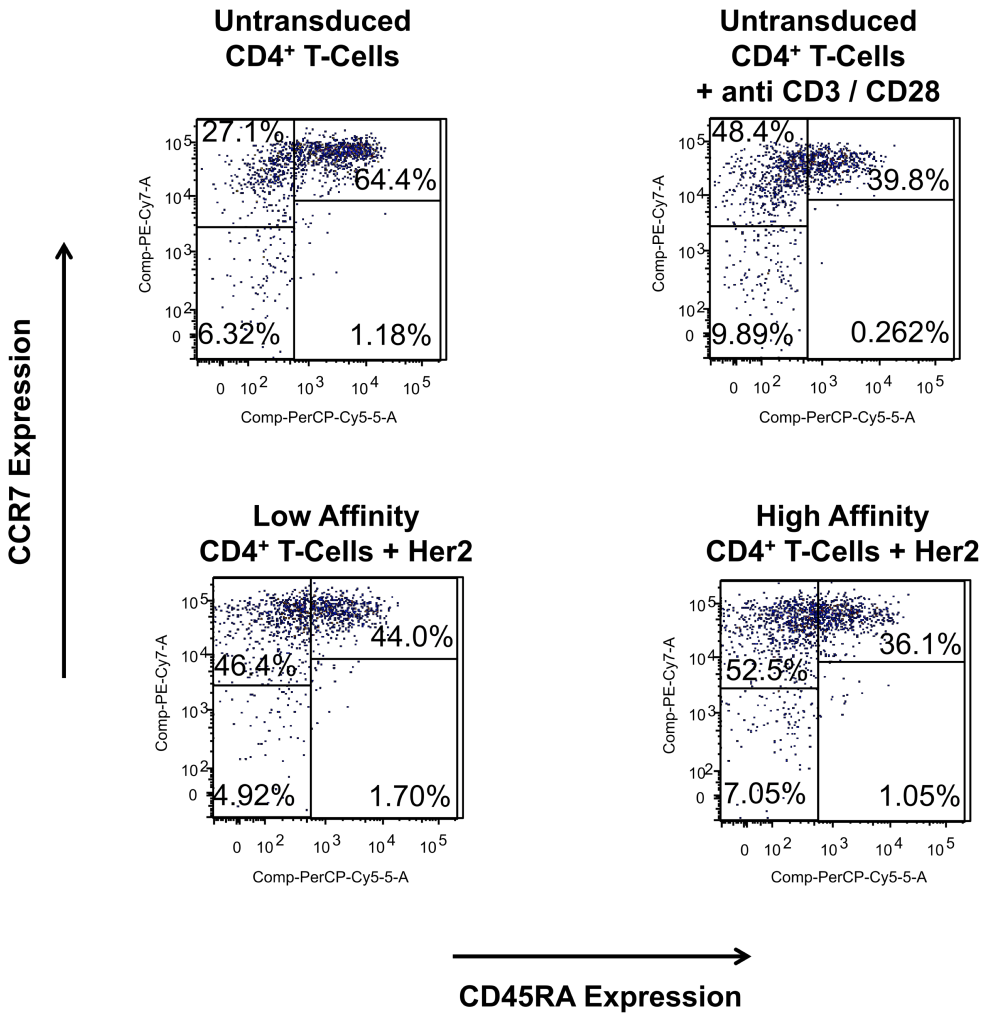


Figure 3.4: Signaling through chimeric antigen receptors polarizes cells towards a central memory phenotype. CD4+ T cells isolated from healthy human donors were transduced with low affinity or high affinity CARs and then allowed to return to a resting state. Cells were then stimulated through the receptor for two days and compared to untransduced cells treated with or without antibodies to CD3 and CD28 at a ratio of 1:1. Analysis was performed 7 days post stimulation, and cells were cultured in IL-7 and IL-2 during the intervening period. The use of CCR7 and CD45RA can be used to classify cells into three distinct populations: CCR7+ CD45RA+ naïve-like cells, CCR7+ CD45RA- central memory cells, and CCR7- CD45RA- effector memory cells. Data is presented as dot plots based on flow cytometry analysis and is from a representative experiment that has been performed three times with different donors.

T Cell Signaling at the Time of HIV-1 Infection Regulates Provirus Expression

To determine whether T cell signaling influences viral infection, Jurkat T cells expressing low affinity or high affinity CARs were plated on Her2-coated wells and simultaneously infected with VSV-G pseudotyped NL4-3.Luc, a single-cycle HIV-1 clone which contains a luciferase reporter gene in place of *nef*. VSV-G or Vesicular Stomatitis Virus Envelope Glycoprotein G allowed me to bypass potentially confounding effects from receptor/chemokine receptor signaling due to gp120 binding (Davis *et al.*, 1997) and focus specifically on CAR-associated signaling cascades. To assess whether signaling influenced the establishment of infection, I measured levels of HIV-1 proviral DNA using a previously described nested *Alu*-PCR approach (Agosto *et al.*, 2007). I modified the assay by designing primers to the luciferase open reading frame to estimate the relative frequency of HIV-1 integration without confounding signals from the lentiviral vectors used to express the CARs (see Chapter 2). CAR-associated signaling did not affect the infection of Jurkat cells since I detected comparable numbers of proviruses regardless of the presence or absence of CAR ligand (Figure 3.5A). When HIV-1 expression was measured by luciferase activity, Jurkat cells infected in the context of strong CAR signaling expressed greater than 10-fold more HIV-1 compared to untreated controls (Figure 3.5B). In contrast, engagement of the low affinity CAR led to a modest 3-fold expression compared to unstimulated cells despite a similar proviral load as the high affinity CAR-expressing cells. These data indicate that strong T cell signaling at the time of infection facilitates HIV-1 expression without enhancing provirus integration.

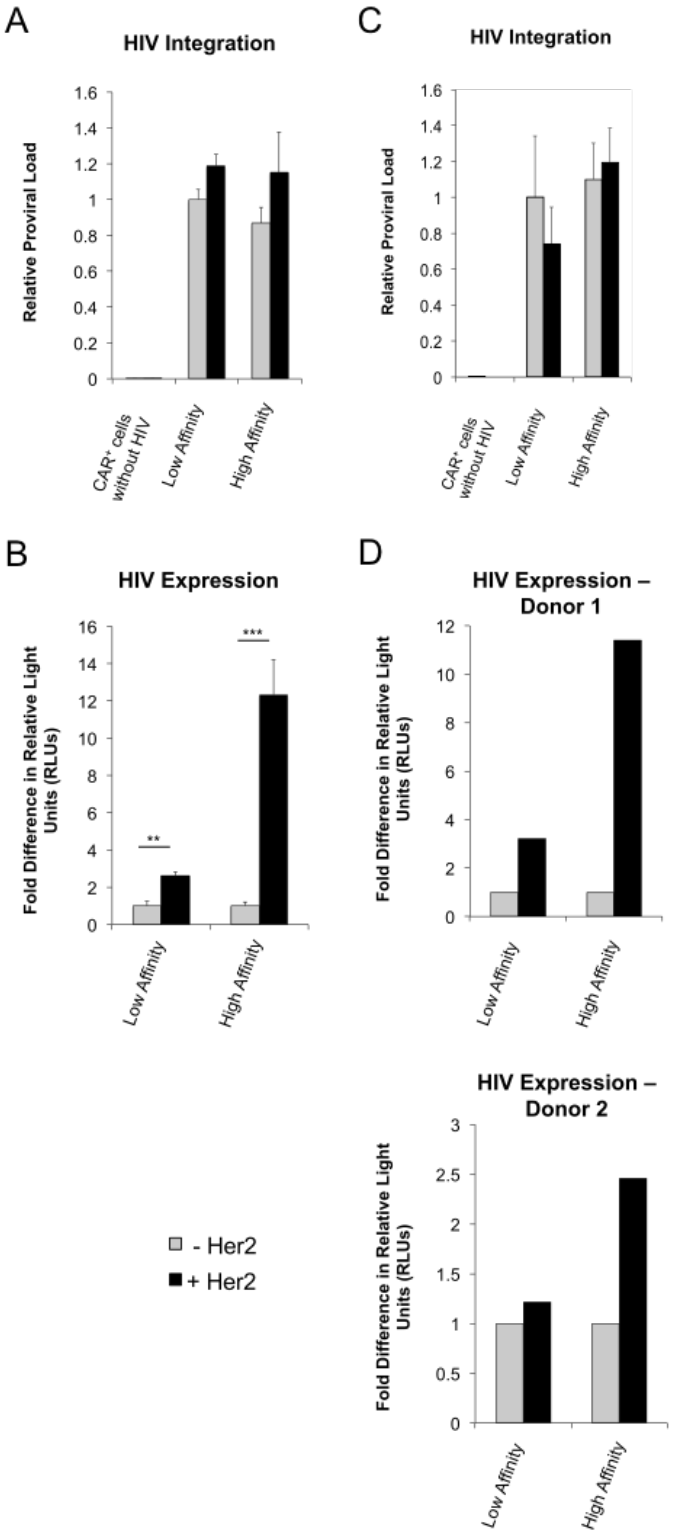

A
HIV Integration
Relative Proviral Load
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
CAR+ cells without HIV
Low Affinity
High Affinity
C
HIV Integration
Relative Proviral Load
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
CAR+ cells without HIV
Low Affinity
High Affinity
B
HIV Expression
Fold Difference in Relative Light Units (RLUs)
16
14
12
10
8
6
4
2
0
**
***
Low Affinity
High Affinity
D
HIV Expression – Donor 1
Fold Difference in Relative Light Units (RLUs)
12
10
8
6
4
2
0
Low Affinity
High Affinity
HIV Expression – Donor 2
Fold Difference in Relative Light Units (RLUs)
3
2.5
2
1.5
1
0.5
0
Low Affinity
High Affinity
- Her2
+ Her2

Figure 3.5: T cell signaling at the time of HIV-1 infection regulates provirus expression.
(*A* and *B*) Jurkat T cells were transduced with the high or low affinity CAR. Cells were stimulated through the CAR at the time of HIV-1 infection with VSV-G pseudotyped NL4-3.Luc. (*A*) Relative levels of integrated provirus 24 h post infection of high or low affinity Jurkat T cells using nested *Alu*-PCR. Uninfected CAR-expressing Jurkat T cells were a negative control. (*B*) Luciferase activity measured 24 h post-infection presented as fold difference in relative light units (RLUs) over unstimulated cells for each CAR+ cell line. **$p<0.005$,***$p\leq0.0005$. *A* and *B* were performed in triplicate and are representative of four independent experiments. Data are presented as mean ± standard deviation. (*C* and *D*) Primary $CD4^+$ T cells isolated from healthy human donors were transduced with CARs and given one week to return to a resting state. Cells were stimulated through the CAR at the time of HIV-1 infection with single-round VSV-G pseudotyped NL4-3.Luc. (*C*) Relative levels of integrated provirus 24 h after infection of high or low affinity CAR-expressing primary T cells (from the same donor) using nested *Alu*-PCR. Uninfected CAR-expressing primary T cells were a negative control. Results are from a single experiment performed in triplicate and are representative of two independent experiments. Data are presented as mean ± standard deviation. (*D*) Luciferase activity measured 4 days post infection presented as fold difference in RLUs over unstimulated cells for each CAR+ cell line. Experiments from two separate donors are shown and are representative of three independent experiments. See also Figure 3.6 and 3.7.

I confirmed that these differences were due to downstream signaling cascades emanating from the CARs by using the Src kinase inhibitor, PP2. Src kinases are the first downstream targets of T cell receptor activation and are recruited to the phosphorylated ITAMs (Gibson *et al.*, 1996; Rossy *et al.*, 2013). In the presence of PP2, the increase in HIV-1 expression upon CAR stimulation was attenuated, consistent with T cell signaling as a regulator of HIV-1 expression (Figure 3.6). The pharmacologically inactive version of this inhibitor, PP3, had no effect on the ability of CARs to influence HIV-1 expression.

To confirm that differences in luciferase activity were a result of transcriptional upregulation and not post-transcriptional events, I examined production of spliced viral mRNAs in HIV-1 infected CAR-expressing Jurkat T cells. A major impediment to successful HIV-1 replication occurs at the level of splicing (Yukl *et al.*, 2018). I analyzed infected Jurkat cells to measure whether increased cellular activation resulted in increased expression of fully-spliced and partially-spliced viral transcripts. RT-PCR confirmed that increased cellular activation resulted in not only greater levels of fully-

spliced RNA transcripts but also partially-spliced transcripts (Figure 3.7). Although differences were detected between the amount of partially-spliced and fully-spliced mRNAs, this effect was most likely due to primer binding efficiencies or splicing kinetics (Klotman *et al.*, 1991; Puray-Chavez *et al.*, 2017). In addition, not all products are spliced in equal ratios, with *env* transcripts being relatively highly expressed (Ocwieja *et al.*, 2012). Regardless, the fact that all measured spliced products increased upon greater T cell stimulation indicated that transcription was the limiting step of HIV-1 expression in response to TCR signaling.

I validated the observation that signal strength influenced HIV-1 replication and transcription using primary CD4+ T cells that were transduced with either the low affinity or high affinity CAR. Following transduction, cells were allowed to return to a resting state as monitored by low CD69 expression before infection with HIV-1 in the absence or presence of the ligand Her2. Consistent with the data from Jurkat cells, similar levels of proviral DNA were detected in primary CD4+ T cells regardless of the strength of CAR signaling (Figure 3.5C). Cells that received robust stimulation at the time of infection expressed 1.5- to 4-fold more HIV-1 than cells stimulated through the low affinity receptor (Figure 3.5D).

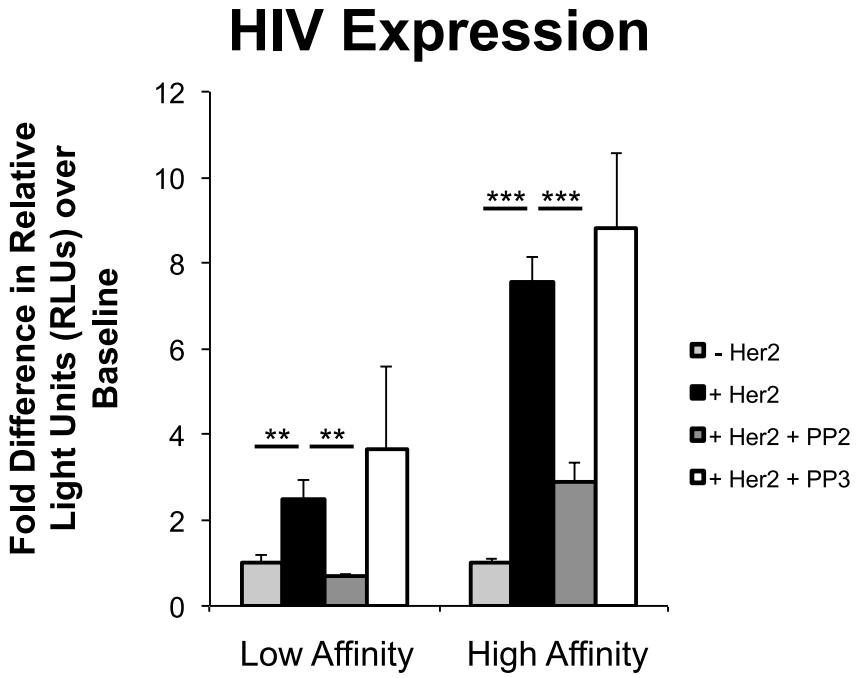


Figure 3.6: Src kinase inhibitor PP2 inhibits CAR-mediated HIV-1 transcription. CAR+ Jurkat T cells were stimulated with or without Her2 in the absence or presence of 10μM PP2 or PP3 at the time of HIV-1 infection with single-round VSV-G pseudotyped NL4-3.Luc. 24 h post infection, cells were lysed to measure luciferase. Data are presented as fold difference in RLUs over unstimulated cells for each CAR+ population. **$p<0.005$, ***$p\leq0.0005$. Figure 3.6 was performed in triplicate and is representative of five independent experiments. Data are presented as mean ± standard deviation.

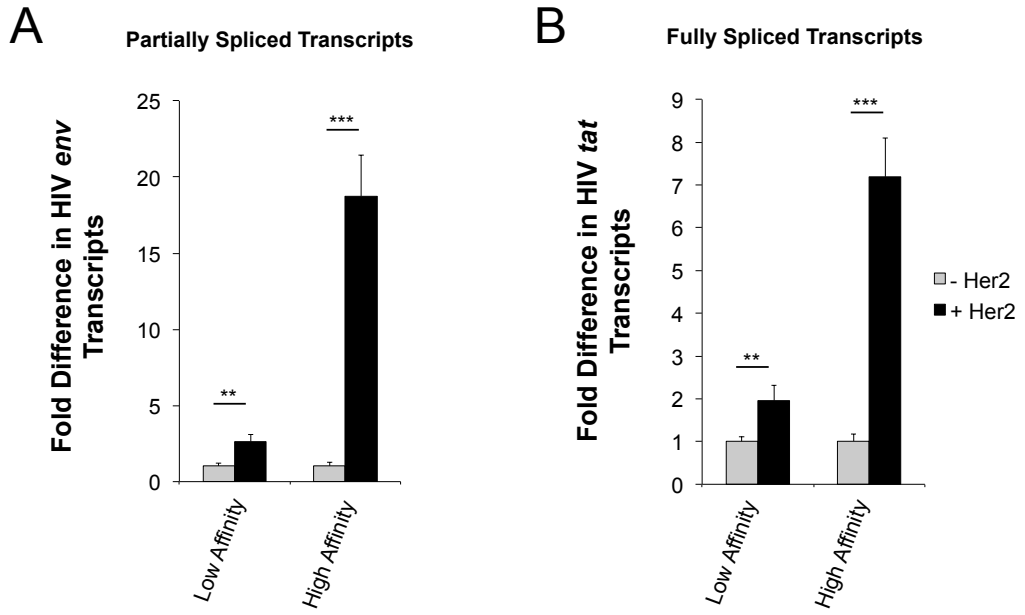


Figure 3.7: T cell signaling at the time of HIV-1 infection regulates provirus expression by inducing transcription. (*A* and *B*) CAR+ Jurkat T cells were stimulated with or without Her2 at the time of HIV-1 infection with VSV-G pseudotyped NL4-3.Luc. 24 h post infection, cells were lysed in order to measure HIV-1 transcripts by qRT-PCR. (*A*) Fold difference in HIV-1 *env* transcripts over corresponding unstimulated conditions as an indication of production of partially spliced RNAs. Although *env* gene is heavily deleted in provirus, the 5' end of the gene remains intact. (*B*) Fold difference in HIV-1 *tat* transcripts over corresponding unstimulated conditions as an indication of production of fully spliced RNAs. **p<0.005,***p<0.0005. *A* and *B* were performed in quadruplicate. Data are presented as mean ± standard deviation.

To gain insight into whether there is a threshold or minimal T cell signal required for HIV-1 infection and replication, I transduced Jurkat T cells with CAR receptors that spanned a range of binding affinities (Figure 3.1B). These cells were infected with NL4-3.Luc as described above in the absence or presence of Her2. Although the high affinity condition supported HIV-1 infection and transcription, the intermediate and low affinity receptors did not support HIV-1 expression (Figure 3.8A). This was despite similar levels of infection as determined by measuring proviral DNA (Figure 3.8B). These data suggest

that T cell signaling controls HIV-1 expression by a digital on/off mechanism since viral expression does not linearly correlate with signal strength.

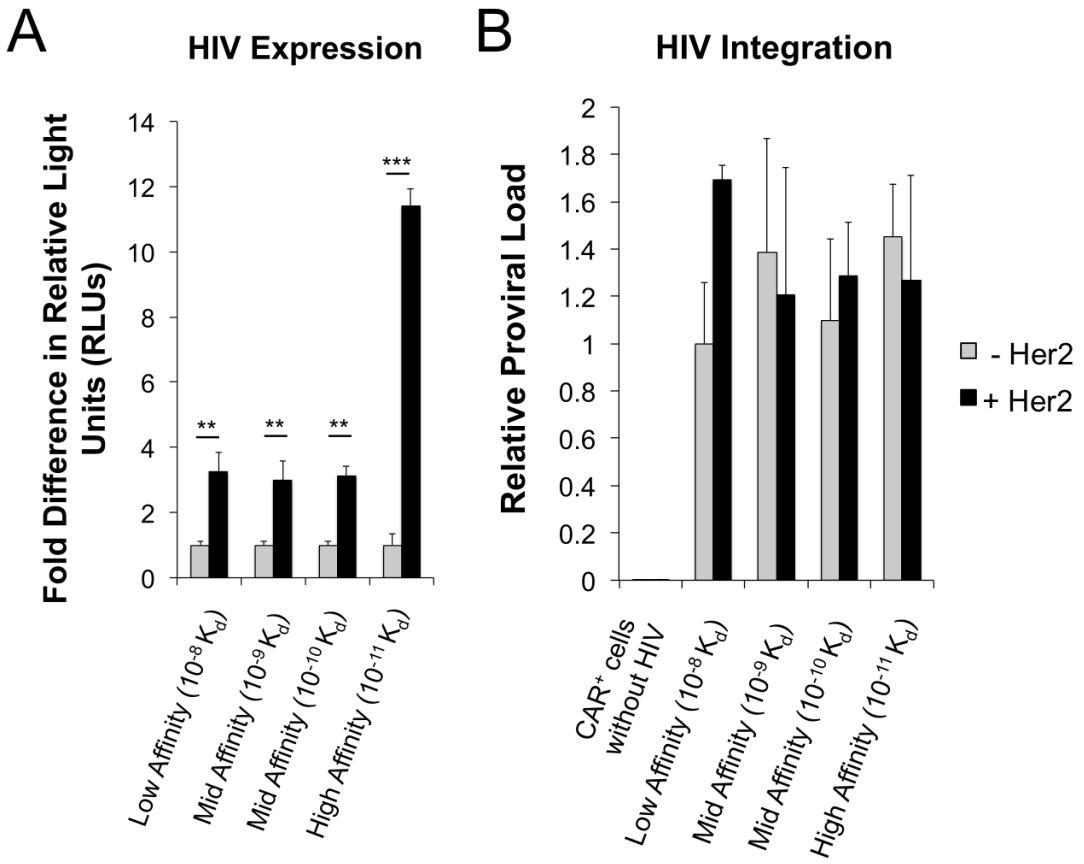


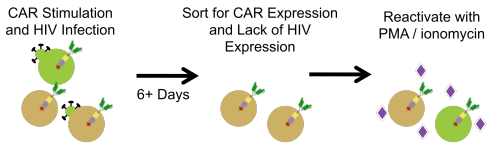
Figure 3.8: Robust T cell signaling is required for HIV-1 transcription. (*A*) Jurkat T cells were transduced and positively selected for indicated CARs and then infected with NL4-3.Luc. 24 h post infection, cells were lysed for luciferase analysis. Data are presented as fold difference in RLUs over unstimulated cells for each CAR+ population. **p<0.005, ***p<0.0001. (*B*) Relative levels of integrated provirus after infection of CAR-expressing Jurkats using nested *Alu*-PCR. *A* and *B* were performed in triplicate and are representative of four independent experiments. Data are presented as mean ± standard deviation.

Robust Signals During HIV-1 Infection Establishes an Inducible Latent Reservoir

I hypothesized that differential T cell signaling during infection alters the size of the inducible latent reservoir. To examine this, I infected CAR-expressing primary CD4+ T cells with VSV-G pseudotyped Bru-dENV-GFP (GFP-expressing single cycle HIV-1) in the presence of Her2 ligand. One week post infection, cells were sorted for both mCherry expression as a marker for CAR transduction and lack of GFP expression in order to enrich for latently infected cells. CAR^{+}/GFP^{neg} cells were reactivated with PMA plus ionomycin or left unstimulated to control for spontaneous HIV-1 reactivation (Figure 3.9A). PMA, a phorbol ester, and ionomycin, a calcium ionophore, engage two separate arms of the T cell activation pathway. PMA and ionomycin significantly reactivated HIV-1 expression within cells that had been initially infected in the context of strong signaling, resulting in a 3- to 9-fold increase in the percentage of GFP positive cells and a 1000-fold induction of HIV-1 mRNA measured by qRT-PCR (Figure 3.9B and 3.9C). However, the observed reactivation of HIV-1 was modest in cells infected at the time of stimulation through the low affinity CAR. A 200-fold induction of HIV-1 RNA was detected in reactivated latently infected cells expressing low affinity CARs, and less than a 2-fold change was observed in the percentage of GFP^{+} cells. Therefore, despite both minimal and robust signaling resulting in comparable amounts of integrated HIV-1 provirus, robust signaling was not only necessary for active transcription but also supported the generation of a population of latently infected cells that could be readily induced to express HIV-1. The population of latent cells generated in response to weaker

CAR signaling was more resistant to reversal suggesting that HIV-1 in these cells was strongly repressed.

A



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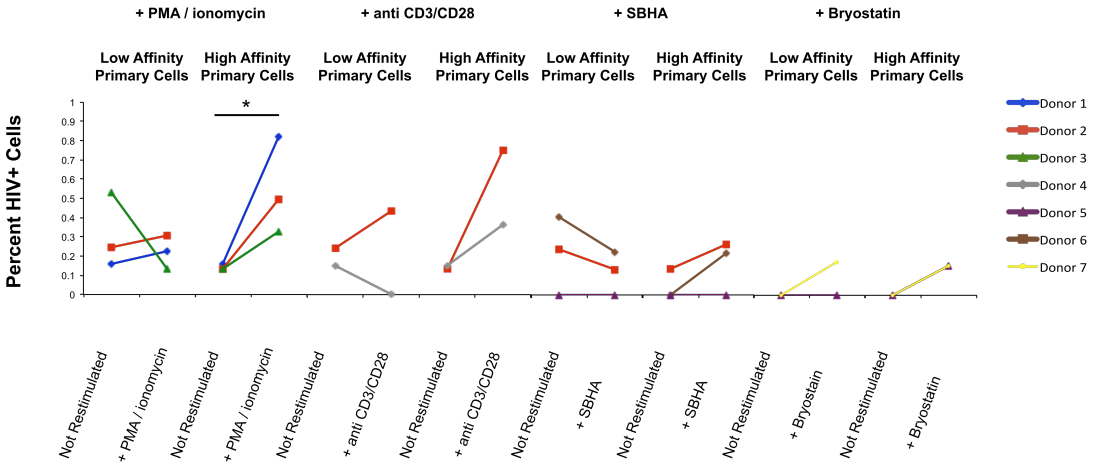


C

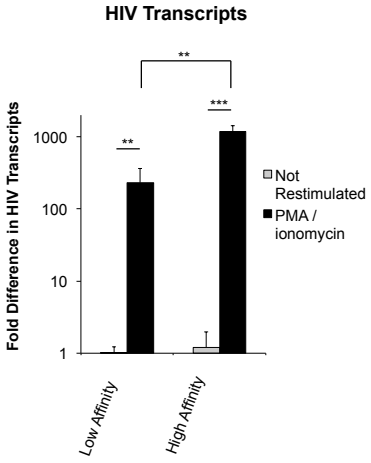


Figure 3.9: Robust signals during HIV-1 infection establish an inducible latent reservoir. (*A*) Outline of experimental plan to enrich for latently infected cells following infection. Primary CD4+ T cells are infected with BRU-dEnv-GFP and GFP-negative cells are sorted to enrich for latently infected cells. (*B*) Percent GFP+ HIV-expressing cells after stimulation of latent cells with various latency-reversing agents: PMA plus ionomycin, antibodies to endogenous CD3 and CD28, SBHA, and Bryostatin. Data are from seven separate donors, and each form of LRA stimulation was performed on cells from 2-3 donors. (*C*) Latently-infected cells were restimulated with PMA and ionomycin. HIV-1 expression was monitored by measuring Tat RNA by qRT-PCR. Values are shown as fold difference in HIV-1 transcripts over corresponding non-reactivated controls. All data in *C* are derived from 4-6 replicates and are representative of three independent experiments with different donors. Data are presented as mean ± standard deviation. *$p<0.05$, **$p<0.005$, ***$p<0.0001$.

I also used other common latency-reversing agents in order to determine if targeting alternative activation pathways could reverse the refractory nature of the low stimulation cells. Antibodies to CD3 and CD28, which would engage the endogenous T cell receptors and fully re-activate these cells, failed to reverse the repressed virus in cells that expressed the low affinity CAR. SBHA (an HDACi) and bryostatin (a PKC agonist) failed to significantly reactivate cells that had received either high or low levels of stimulation at the initial time of infection. (Figure 3.9B).

RNAPII Processivity Limits HIV-1 Transcription in the Absence of Robust Signaling

I was interested in mechanisms that governed HIV-1 repression following integration in the absence of sufficient T cell signaling; therefore, I examined the binding of transcriptional regulators on the HIV-1 LTR by chromatin immunoprecipitation (ChIP). Jurkat T cells expressing low or high affinity CARs were infected with NL4-3.Luc in the absence or presence of Her2 ligand. One day post-infection, cells were fixed and chromatin was prepared for ChIP.

Since HIV-1 proviral latency correlates with a positioned nucleosome that is downstream of the transcriptional start site, I explored whether the LTR was associated with post-translationally modified histones as an indicator of chromatin organization. ChIPs for acetylated histone H3 showed no significant difference in binding of the HIV-1 LTR between cells infected in the absence or presence of T cell signaling (Figure 3.10A). Taken together with the lack of effect of histone deacetylase inhibitors on latency reversal (Figure 3.9B), it would seem that chromatin accessibility does not appear to be limiting HIV-1 proviral transcription during the early stages of infection.

I then examined RNAPII processivity by measuring RNAPII occupancy at multiple points in the HIV-1 proviral genome, including the transcriptional start site and downstream in the HIV-1 *tat* gene. RNAPII was detected at the HIV-1 transcriptional start site whether cells were activated through a CAR or were unstimulated (Figure 3.10B). However, signaling through the high affinity receptor resulted in an increase in downstream RNAPII by greater than 4-fold, whereas only modest levels of RNAPII were found downstream in the absence of signals or following weak signaling (Figure 3.10C).

Since these data indicated a role for transcriptional pausing, I examined if CAR signaling altered the presence of the pausing factor NELF at the HIV-1 transcriptional start site. Using ChIPs, I determined that signaling through the high affinity receptor diminished binding of NELF at the HIV-1 LTR by greater than 85% (Figure 3.10D). These data support a model in which a lack of robust T cell signaling limits HIV-1 transcription by establishing a paused polymerase complex.

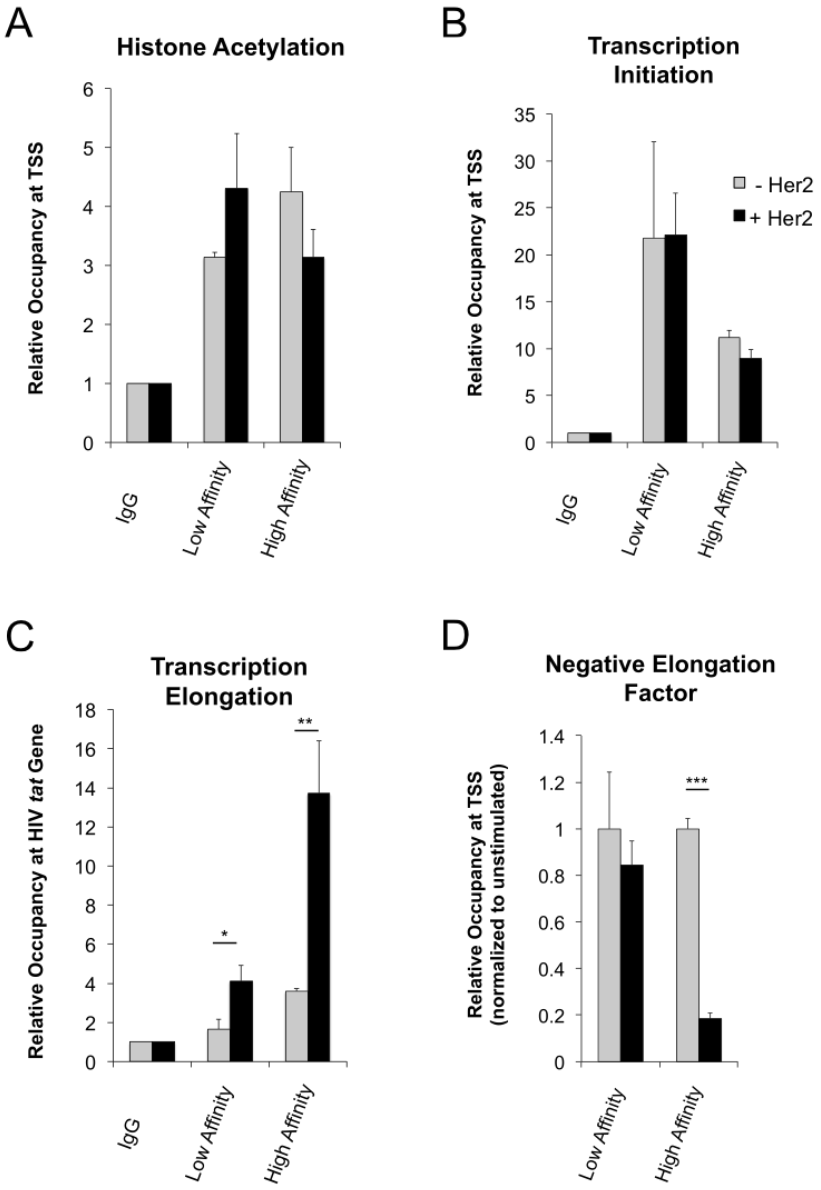


Figure 3.10: RNAPII processivity limits HIV-1 transcription in the absence of robust signaling. CAR-expressing Jurkat T cells were infected with single-round VSV-G NL4-3.Luc and simultaneously plated with or without Her2 ligand. 24 h later, cells were fixed for chromatin immunoprecipitation. (*A*) ChIP for presence of acetylated H3 near the transcriptional start site (nuc-1). (*B*) ChIP for RNAPII at the HIV-1 transcriptional start site. (*C*) ChIP for RNAPII associated with the HIV-1 *tat* gene to measure polymerase processivity. Data from *A-C* are normalized to corresponding IgG controls for each stimulation condition. (*D*) ChIP for NELF-d at the HIV-1 transcriptional start site. Data is normalized to corresponding unstimulated condition for each CAR+ cell line. *A-D* were performed in triplicate and are representative of at least three independent experiments in Jurkat T cells. Data are presented as mean ± standard deviation. Primers used for HIV-1 transcriptional start site are +30 and +239. Primers used for *tat* gene are +5379 and +5482. *$p<0.05$, **$p<0.005$, ***$p\leq0.0005$

DISCUSSION

Previous studies suggest that cell signaling may be a key regulator of HIV-1 expression and latency. The latent reservoir is enriched for antigen specific T cells, including those that respond to CMV, HSV, tuberculosis, and HIV (Douek *et al.*, 2002; Demoustier *et al.*, 2002; Casazza *et al.*, 2009; Geldmacher *et al.*, 2010; Hu *et al.*, 2016). Furthermore, the use of superantigens during viral entry increases HIV-1 replication (Laurence, Hodtsev and Posnett, 1992). Partial activation, cellular polarization, cell-to-cell contact, and/or infection of resting quiescent cells through perturbation have also been suggested to bias infections towards latency (Agosto and Henderson, 2018; Saleh *et al.*, 2007; Bosque and Planelles, 2009; Pace *et al.*, 2011; Agosto *et al.*, 2018; Kumar *et al.*, 2018). Therefore, the extent of cell activation is a key determinant in regulating the course of HIV-1 infection including the formation of the reservoir.

I have shown that differential signaling through CARs, which mimic TCR signaling, influences HIV-1 transcription and latency. In the lymph node, the primary site for both HIV-1 replication and the persistent latent reservoir (Biberfeld *et al.*, 1986; Shen *et al.*, 2003; Aid *et al.*, 2018), T cells sample lymph node resident antigen presenting cells in search for antigen. Some of these interactions, facilitated by the presentation of the T cell cognate antigen, will result in robust T cell activation, clonal expansion, and changes in gene expression. However, most MHC complexes will lack cognate antigen and initiate weak signaling (Zehn, Lee and Bevan, 2009; Martinez *et al.*, 2016). Using multiple CARs whose affinities for the Her2 ligand span several logs, I delivered a range of signaling inputs to model the spectrum of T cell receptor signaling events. My data

indicates that stronger T cell activation at the time of infection, which would be akin to antigen-specific responses, correlates with robust HIV-1 expression as well as the establishment of inducible latently infected cells. I do not address here the possibility that additional factors may compensate for suboptimal T cell receptor signaling. Interactions with antigen presenting cells would engage a number of costimulatory molecules and inhibitory receptors. In addition, the presence of inflammatory cytokines, such as would be expected during the acute stages of HIV-1 infection, may alter the level of cellular activation. Whether the ability of T cell stimulation to regulate HIV-1 is a matter of quality or simply quantity of signal should be examined further.

Having a library of CARs with a range of binding affinities allowed me to determine if HIV-1 responds to signaling in an analog fashion correlating with signal input or digitally regulated by specific thresholds resulting in all-or-none responses (Zikherman and Au-Yeung, 2015). Signaling through the CARs with affinities that were intermediate did not support active transcription despite a greater than 10-fold increase in binding affinity compared to the low affinity receptor. These results would suggest that TCR signaling provides more of an on/off switch and that there exist signaling thresholds that must be overcome to assure efficient transcription and replication.

Signal transduction and gene expression are inherently noisy processes, and stochastic events are hypothesized to drive HIV-1 latency. That latency and HIV-1 replication are driven by episodic bursts of proviral transcription and Tat levels has been supported by mathematical modeling and experiments using engineered virus models (Burnett *et al.*, 2009; Donahue *et al.*, 2012; Razooky *et al.*, 2015). Even if latency is

driven by random fluctuations of provirus transcription, T cell associated signals are strong modulators of noise, and targeting these pathways could enhance treatments directed at HIV-1 reactivation (Dar *et al.*, 2014). However, it is important to appreciate that although signaling and transcription are subject to stochastic variation, these are coordinated and combinatorial processes that lead to defined patterns of gene expression and phenotypic outcomes (Banos, Agelopoulos and Thanos, 2013).

Regulated aspects of transcription include assembly of multi-subunit complexes such as RNAPII and associated cofactors, chromatin, and transcription factors at the LTR. Figure 3.10 suggests that the association of NELF with RNAPII is regulated by TCR signaling. Multiple positive and negative signals are known to converge on NELF-driven transcriptional pausing. P-TEFb relieves NELF repression through phosphorylation (Fujinaga, *et al.*, 2004) and is itself regulated by cellular stress and signals (Garriga *et al.*, 1998; Zhou and Yik, 2006; Fujinaga *et al.*, 2015).

My data regarding the lack of histone acetylation as a block to transcriptional elongation at the time of viral integration is in marked contrast to its acknowledged role in the maintenance of HIV-1 latency in chronically infected cell lines and patient samples *ex vivo* (He and Margolis, 2002; Archin *et al.*, 2009). However, our lab has shown that NELF interacts with co-repressors including NCoR1-GPS2-HDAC3 at the HIV-1 promoter (Natarajan *et al.*, 2013) which may reinforce HIV-1 latency, especially during chronic infection, by facilitating post-translational modifications of histones and chromatin organization.

I propose that strength of signal at the time of infection acts as a bifurcating event leading to *either* robust transcription and the establishment of an inducible latent reservoir *or* minimal transcription and deep-seated latency (Illustration 3.1). My observations are consistent with the previous characterization of patient reservoirs that identified three subsets of latently infected cells: a small population of cells carrying inducible provirus, larger populations of cells with intact proviruses that are difficult to reactivate, and many defective proviruses (Ho *et al.*, 2013). Successful purging of the latent reservoir may require the use of a cocktail of latency reversing agents or the development of novel strategies to block reactivation (Xing and Siliciano, 2013; Darcis *et al.*, 2015; Darcis *et al.*, 2017).

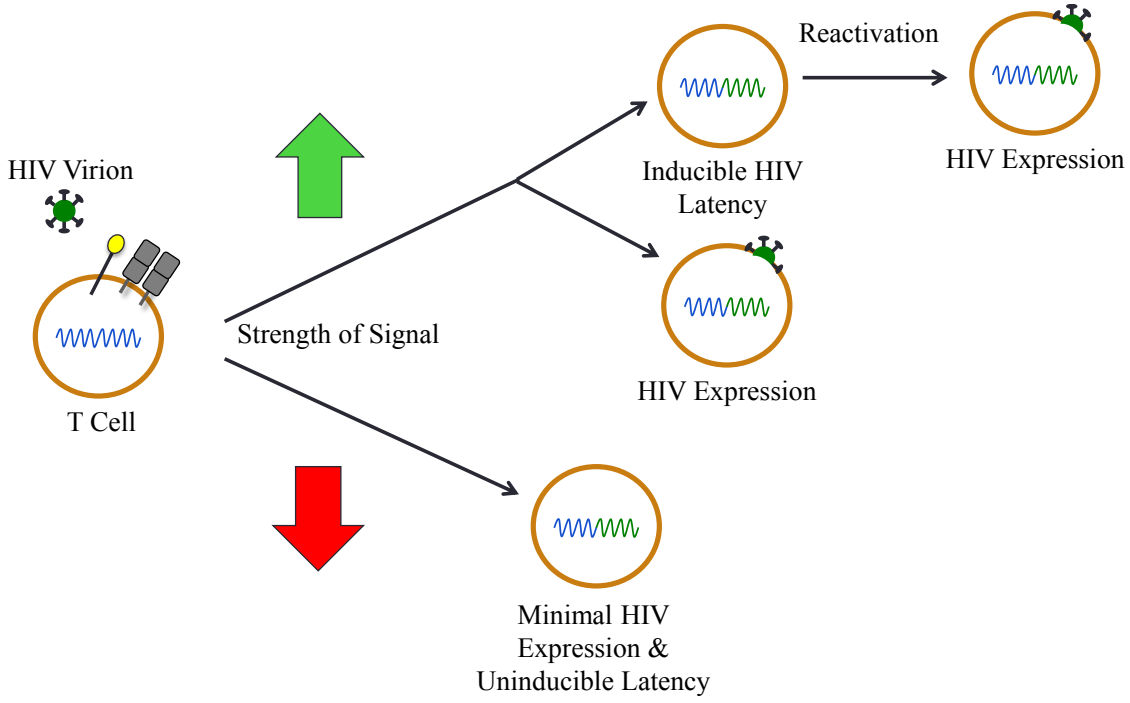


Illustration 3.1: T cell signaling during HIV-1 infection drives viral fate. Amplitude of TCR signaling cascade polarizes cells towards a favorable environment for productive HIV-1 infection and the formation of a readily inducible latent reservoir or an unfavorable environment for viral replication marked by uninducible latency.

CHAPTER FOUR: NUCLEASE-DEFICIENT CAS9-KRAB CAN BE USED TO SILENCE HIV-1 EXPRESSION THROUGH REDUCTION IN RNAPII INITIATION

INTRODUCTION

Discovery of CRISPR-Cas9 and Use as an HIV-1 Therapeutic

CRISPR-Cas9 offers significant advantages over other strategies for gene editing. TALENs (transcription activator-like effector nucleases) and zinc finger nucleases were widely considered the most accurate molecular tools to target specific sections of the genome (Miller *et al.*, 2007; Mussolino *et al.*, 2011), but the application of a CRISPR-based approach heralded a new era in gene editing. In 2013, the laboratories of Feng Zhang and George Church simultaneously demonstrated that a Cas9 system adapted from *Streptococcus pyogenes* could be used for genome editing in both cell lines and induced pluripotent stem cells (Cong *et al.*, 2013; Mali *et al.*, 2013). Both approaches were based on the capacity of the bacterial CRISPR system to excise foreign DNA and insert it between the palindromic repeats in a region known as the protospacer. This protospacer is then cleaved, along with an adjoining portion of the palindrome, inserted into CRISPR Associated Protein 9, and recruited to its complementary sequence located within an invading pathogen (Mali, Esvelt and Church, 2013). It should also be pointed out that any corresponding DNA sequence must be immediately upstream from a Protospacer Adjacent Motif (PAM) site. The PAM specific sequence for Cas9 isolated from

Staphylococcus aureus, the bacterial species used for some of the experiments outlined in this chapter, is 5'-(N)NGRRT-3'. N refers to any nucleotide, while R denotes a purine base (Xie *et al.*, 2018).

By operating under these particular requirements, the exonuclease is directly targeted to a specific gene with minimal off-target effects (Kim *et al.*, 2015). By providing their own protospacer sequence in the form a small guide RNA (sgRNA), the Church and Zhang labs were able to redirect the CRISPR system to bind to and excise a human gene of interest.

An immediate application of CRISPR-based gene editing was its potential as an HIV-1 therapeutic. Since HIV-1 persists as transcriptionally silent latent proviruses, CRISPR provides a possible mechanism that could be used to excise integrated HIV-1. The Khalili lab first demonstrated the capacity of CRISPR to remove integrated proviruses through the use of guide RNAs directed towards the U3 region of the HIV-1 LTR (Hu *et al.*, 2014). However, significant questions still remain regarding method of delivery *in vivo*, off-target effects (which, although minimal, could still pose significant health concerns), complete removal of all latent proviruses, and viral escape (Fu *et al.*, 2013; Wang G *et al.*, 2016; Wang Z *et al.*, 2016; Mout *et al.*, 2017). The Khalili lab performed *in vivo* experiments using humanized mice infected with HIV-1, but failed to completely excise all HIV-1 DNA. In addition, significant targeting differences were seen between various tissue sites, with reduced efficacy in the central nervous system (Kaminski *et al.*, 2016).

For these reasons, I propose the use of a nuclease-deficient Cas9 to recruit chromatin-modifying factors to the HIV-1 provirus instead of degrading the genome. This approach provides the additional benefit of removing any immune pressure resulting in viral escape as in theory no transcription and thus no replication would occur at all. New efforts at the use of adeno-associated vectors as a delivery system could bypass the current issues with cellular penetrance and might allow the system I describe here to be brought into the clinic (Platt *et al.*, 2014).

Cas9-KRAB Construct for Targeted Gene Repression

The first attempts to fuse a nuclease-deficient Cas9 to a Krüppel Associated Box Domain was first described by the Wang and Gersbach labs in the mid-2010's (Lawhorn, Ferreira and Wang, 2014; Thakore *et al.*, 2015). KRAB domains are known to bind to the endogenous host factor, Kap1 or KRAB-Associated Protein-1, which together target various repressors to the region of the genome to which the KRAB domain is bound. These repressors include histone deacetylases, histone lysine-methyltransferases, and DNA methyltransferases. As a result, the surrounding genes become silenced, and we can detect both the spreading of marks associated with heterochromatin and a lack of transcription (Friedman *et al.*, 1996; Groner *et al.*, 2010; Oleksiewicz *et al.*, 2017). It is hypothesized that KRAB-Kap1 may mediate this transcriptional effect through directly dislodging the RNAPII complex (Moosmann *et al.*, 1997; Groner *et al.*, 2010).

Most KRAB-containing proteins have been described in mouse embryonic cells, such as the zinc-finger protein ZFP809 that can repress murine leukemia virus and

murine endogenous retroviruses (Wolf and Goff, 2009; Wolf *et al.*, 2015). The human KRAB-containing zinc-finger protein ZNF93 has recently been discovered as a restriction factor for the long interspersed nuclear element 1 or L1 in human embryonic stem cells (Jacobs *et al.*, 2014). KRAB-Kap 1 has consistently been shown to play an important role in cellular gene regulation and its adaptation to the CRISPR-Cas9 system offers a novel approach to targeted epigenetic editing.

My goal was to introduce a nuclease-deficient Cas9-KRAB domain construct into cells at the time of infection with HIV-1. Together with sgRNAs directed against regions of the HIV-1 genome immediately upstream of the appropriate PAM site, our lab was able to successfully repress HIV-1 expression. We further illustrated the potential of this nuclease-deficient Cas9 system by electroporating it into latently infected T cells. The exonuclease was capable of preventing viral reactivation, highlighting its prospective role as an HIV-1 therapeutic. In this way, I aimed to bias an infection towards long-term transcriptional repression or inactivation.

RESULTS

Nuclease-Deficient Cas9-KRAB Suppresses HIV-1 Expression

I obtained nuclease-deficient Cas9-KRAB plasmids from the Wilson Wong laboratory at Boston University. They created two separate fusion constructs, one based on *Staphylococcus aureus* and a second on *Streptococcus pyogenes*. Although the dsaCas9 is more specific due to its more stringent PAM sequence, dspCas9 is more

widely used and was the first variant isolated by the Church and Zhang labs. One sgRNA (dsp361) was modified from a sgRNA described in a paper using a dCas9 fused to an activating domain and overlaps the NF-κB sites in the HIV-1 LTR (Saayman *et al.*, 2016). A separate sgRNA (dsp397) binds to the SP1 site in the LTR (Hu *et al.*, 2014). Alex Olson, a technician in the Henderson lab who performed several of the experiments described in this chapter, identified a panel of dsaCas9 guide RNAs that would bind to the NL4-3 HIV-1 sequence using the online tool Benchling (Illustration 4.1) (Benchling, 2019). These sgRNAs span the proviral genome.

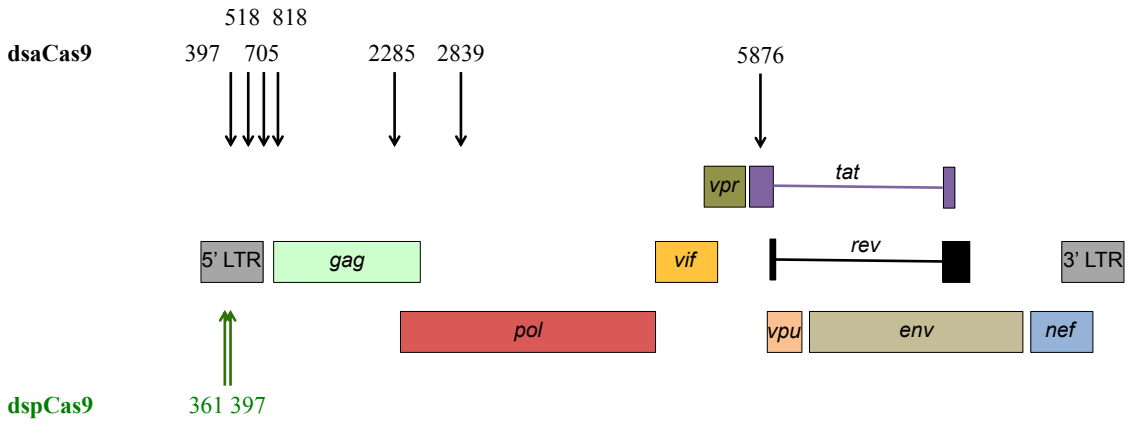
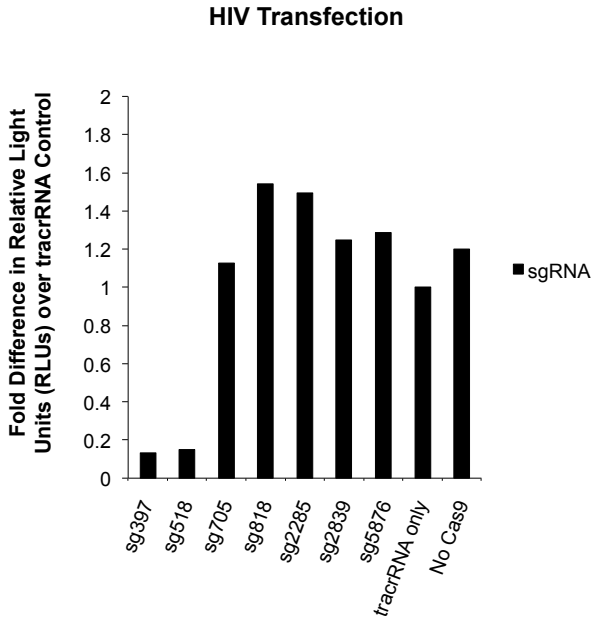


Illustration 4.1: Selection of HIV-1 binding sgRNAs for CRISPR-mediated epigenetic silencing. Binding sites were selected using the online tool Benchling that spanned the HIV-1 genome, including sites in the LTR, *gag-pol*, and *tat*. Schematic based off of a figure modified from (Colin and Van Lint, 2009).

We first cotransfected the DNA sequences encoding for the dsaCas9 sgRNAs with NL4-3.Luc, a singe-cycle luciferase construct, into HEK293T cells and measured luciferase at 48 hours post transfection. Both dsa397 and dsa518, located within the HIV-1 LTR, showed the greatest effect on luciferase repression and we focused primarily on

these guides (Figure 4.1A). We further illustrated the potential of this system to block HIV-1 expression by infecting HEK293T cells with VSV-G pseudotyped NL4-3.Luc while transfecting with dsaCas9. Twenty-four hours later, we transfected cells with plasmids encoding for the sgRNAs and measured luciferase units three days post-infection. We were able to block at least 50% of viral transcription resulting from HIV-1 infection (Figure 4.1B).

A


HIV Transfection
Fold Difference in Relative Light Units (RLUs) over tracrRNA Control
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
sgRNA
sg397
sg518
sg705
sg818
sg2285
sg2839
sg5876
tracrRNA only
No Cas9

B

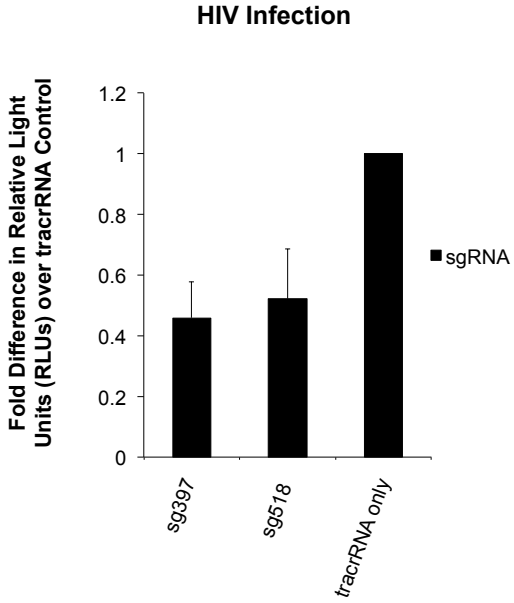

HIV Infection
Fold Difference in Relative Light Units (RLUs) over tracrRNA Control
1.2
1
0.8
0.6
0.4
0.2
0
sgRNA
sg397
sg518
tracrRNA only

Figure 4.1: KRAB binding to the HIV-1 LTR inhibits viral expression. (*A*) HEK293T cells were co-transfected with VSV-G NL4-3.Luc, dsaCas9-KRAB, and the indicated sgRNA. 48 h later, cells were lysed for luciferase analysis. Data are presented as fold difference in RLUs over tracrRNA only control. (*B*) HEK293T cells were infected with VSV-G NL4-3.Luc and simultaneously transfected with dsaCas9-KRAB. 24 h later, cells were transfected with the indicated sgRNA. 48 h post infection, cells were lysed for luciferase analysis. Data are presented as fold difference in RLUs over "tracrRNA only" control and represent mean ± standard deviation. Data in *B* was performed in triplicate. "tracrRNA only" refers to the addition of the sequence corresponding to the tracrRNA without the crRNA sequence necessary to bind HIV-1. "No Cas9" refers to HIV-1 transfection only.

Nuclease-Deficient Cas9-KRAB Prevents Latent HIV-1 Reactivation

J-Lat cells harbor an integrated latent copy of HIV-1 that is responsive to various Tat inducers including TNF-α and phorbol esters (Jordan, Bisgrove and Verdin, 2003; Williams *et al.*, 2007). We thus sought to determine if we could block HIV-1 reactivation in these cells through the use of our nuclease-deficient Cas9 construct. Because J-Lat cells are not easily transfected with plasmids, we used our dspCas9 system, for which we had RNA transcripts of our sgRNAs. Following transduction of the J-Lats with dspCas9 expressed in a lentiviral vector, cells with the exonuclease were enriched through the use of an antibiotic selection marker. We then electroporated the J-Lats with either of the sgRNAs for the *Streptococcus pyogenes* construct. Five days post electroporation, cells were restimulated using TNF-α. Although treatment with the LRA resulted in a baseline 9-fold increase in HIV-1 RNA as measured by qRT-PCR, this was reduced by more than 50% in the samples treated with the sgRNAs (Figure 4.2).

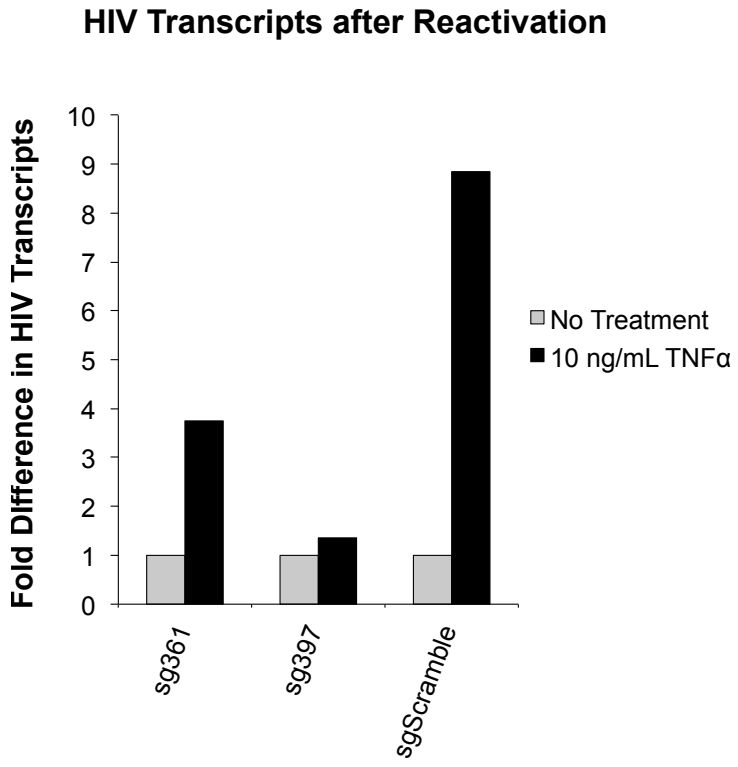


Figure 4.2: KRAB-Kap1 blocks HIV-1 latency reversal in J-Lat cells. J-Lat cells were transduced with a dCas9-KRAB plasmid within a selection vector. Cells were electroporated with sgRNAs indicated above and reactivated with 10 ng/mL TNFα five days post-electroporation. HIV-1 transcription was measured by qRT-PCR using *gag*-specific primers 24 h after stimulation. Values are shown as fold difference in HIV-1 RNA transcripts over corresponding non-reactivated controls. "sgScramble" refers to the selection of a sgRNA not known to bind to any predicted sequence in the human genome.

DISCUSSION

The use of latency-reversing agents to reactivate transcriptionally silent HIV-1 has so far been unable to eradicate the DNA reservoir in any clinical trial. In fact, most HDACi's have failed to result in any detectable reduction in proviral load (Sagot-Lerolle *et al.*, 2008; Archin *et al.*, 2010; Archin *et al.*, 2012). Efforts to permanently suppress

HIV-1 or to bias an infection during the early stages towards latency must be considered as potential therapeutics.

The most challenging aspect to permanent HIV-1 suppression is our ability to specifically target transcriptional host repressors to the provirus. CRISPR-based gene editing provides a substantial improvement over previous strategies, due to the specificity of its binding and the lack of off-target effects. However, the possibility of viral escape poses a major barrier to its successful use as a nuclease. I propose its adaptation, however, to a delivery system in which it can be used to bring binding partners, such as a KRAB domain, to the proviral genome. Other labs have used a nuclease-deficient Cas9 to deliver an activating domain to the HIV-1 LTR (Zhang *et al.*, 2015; Saayman *et al.*, 2016). While this approach seems feasible, the data presented in Chapter 3 illustrates the challenges at reversing latency once established. Host repressors recruit other transcription factors, which in turn target larger complexes such as HDACs, histone methyltransferases, and polymerase-binding factors such as NELF. In concert with one another, large transcriptional networks and scaffolds are formed, resulting in entrenched heterochromatin (Ivanov *et al.*, 2007; Natarajan *et al.*, 2013; Meier and Brehm, 2014). For instance, evidence exists that Kap1 may operate in conjunction with the newly discovered HUSH complex to silence endogenous retroviral elements in mouse embryonic stem cells (Robbez-Masson *et al.*, 2018). HUSH, or the human silencing hub, has been identified as a restriction factor for HIV-1 and HIV-2 expression and is targeted for ubiquitination by the HIV-2 protein Vpx or Viral Protein X (Chougui *et al.*, 2018;

Yurkovetskiy *et al.*, 2018). Future work will need to be performed to determine if HUSH and Kap1 interact directly or indirectly.

The existence of multiple layers of repressive factors that cooperate to silence HIV-1 expression suggests that the reverse strategy of "block and lock" may be viable (Darcis, Van Driessche and Van Lint, 2017). If we can bias latency towards a specific fate, we may be able to achieve a functional cure through intrinsic entrenchment of this repression. My data indicated that guide RNAs directed specifically against the HIV-1 LTR inhibit viral expression. These guides enabled us to suppress HIV-1 transcription shortly after infection and achieve a more than 50% block to latency reversal in chronically infected cells. The differences in efficacy of different guide RNAs indicate that a cocktail of multiple guides may be necessary to repress viral transcription beyond a point where a patient can interrupt therapy. It is not surprising that the most effective guides overlap with specific binding sites in the HIV-1 LTR, perhaps indicating a dual role of KRAB-Kap1 recruitment and a direct steric hindrance to transcription factor binding.

A major challenge to bringing this approach into clinical trials is the method of cellular delivery. However, multiple labs have seen success with adenovirus-based vectors, and I believe that an approach like this may be reasonable (Platt *et al.*, 2014; Kaminski *et al.*, 2016). Because the system described here does not result in gene deletion, I hypothesize that any of the already rare off-target effects will be minimal and that this strategy poses no risk of hereditary gene editing.

CHAPTER FIVE: DISCUSSION AND FUTURE IMPLICATIONS

Summary of Results

The results described within this dissertation highlight the importance of the cellular and local chromatin environments at the time of HIV-1 infection on the fate of the virus. They also enabled me to verify the hypotheses detailed within the Specific Aims that were listed in the first chapter. For Specific Aim 1, I determined the effect of distinct T cell receptor signal strengths at the time of HIV-1 infection on viral expression within primary cells and reactivation of latent proviruses. To study this, I manipulated the cellular activation state through the use of chimeric antigen receptors that mimicked the endogenous T cell receptor. Through the substitution of single chain variable fragments differing in antigen binding affinity, I modulated the strength of signal that a cell received at the time of viral infection. These CARs intersected the native T cell receptor signaling pathways, as demonstrated by similar global transcriptional changes (Figure 3.2) and increased CD69 expression (Figure 3.3). Further evidence of their effects can be seen via the differences observed in acute HIV-1 expression.

Stimulation of CAR-expressing cells with their cognate Her2 antigen resulted in an increase in viral expression, and this response correlated with the strength of cellular activation (Figure 3.5). However, I detected no similar increase in viral integration, implying that the observed effects were due to post-integration events. I further confirmed these results by direct measurement of RNA transcripts and saw a similar pattern as observed with the luciferase analysis (Figure 3.7).

It was reasonable to assume that cells which expressed higher levels of HIV-1 at early time points would be less likely to also harbor inducible latent proviruses since the total number of integrated proviruses was held constant. However, cells that received the greatest amount of stimulation during viral infection were also the most responsive to latency-reversing agents predicted to activate HIV-1 transcription through different biochemical pathways (Figure 3.9).

To address Specific Aim 2, for which I analyzed the transcriptional landscape of the provirus among cell receiving differential stimulation at the time of HIV-1 infection, I performed chromatin immunoprecipitation. I discovered that the local chromatin environment was open and accessible as measured by histone acetylation regardless of cellular activation. This is in agreement with multiple other studies that revealed a bias towards open chromatin that can be attenuated if host factors involved in nuclear import are knocked out or their interactions with HIV-1 capsid are blocked (Wang *et al.*, 2007; Koh *et al.*, 2013; Sowd *et al.*, 2016). The data in Figure 3.10 indicated that successful polymerase processivity only occurred under high activation conditions in concert with release of the pausing factor NELF from the HIV-1 LTR. Based on this evidence, I concluded that although HIV-1 preferentially integrates into regions of open chromatin, the level of global cellular activation regulates whether host repressors are recruited to the provirus. The lack of responsiveness of the virus within minimally activated cells to secondary stimulation suggests that early association with host repressors results in entrenched transcriptional repression and deep-seated latency.

These results led me to hypothesize that I could bias an infection towards deep-seated latency, which was the basis for Specific Aim 3. I hypothesized that I could use a nuclease-deficient Cas9 construct to recruit host repressors to the provirus and suppress HIV-1 expression. By fusing dCas9 to a KRAB domain, we were able to substantially block HIV-1 expression upon transfection with an HIV-1 plasmid and achieved a greater than 50% reduction in viral protein production after infection (Figure 4.1B). In order to determine whether KRAB-Kap1 could induce permanent repression, we electroporated a J-Lat line bearing both a silent copy of HIV-1 along with a nuclease-deficient Cas9 construct with LTR-specific sgRNAs. Treatment of these cells with TNF-α was not sufficient to achieve substantial viral reactivation as it did in the control condition, in which there was a 9-fold increase in viral protein production (Figure 4.2). This experiments listed here confirm my central hypothesis that the global cellular environment at the time of HIV-1 infection determines the potential for inducible latent infection and that this axis can by bypassed by modification of the local chromatin environment.

Latency: A Goal or an Obstacle?

Based on the data detailed in this defense as well as the failure of multiple clinical trials to clear the entire viral reservoir, I propose that a functional cure of HIV-1 cannot be achieved through latency reversal. There is growing evidence that the latent reservoir is not homogenous, but rather a collection of multiple subsets in which latency is both

regulated by different mechanisms and has differing capacities to be re-activated. I have illustrated here that the level of cellular activation at the time of infection may determine whether latently infected cells are inducible or non-inducible. It has been known for some time that significant portions of the viral reservoir are refractory to standard LRAs in spite of their intact genomic content (Ho *et al.*, 2013; Hosmane *et al.*, 2017). I have argued in this dissertation that the cellular conditions at the time of viral entry determine the long-term fate of the virus and their susceptibility to LRAs. Minimal levels of stimulation, which may be sufficient for viral entry and integration, are inadequate to recruit an activating transcriptional network at the time of infection or to remove a repressive network during secondary stimulation.

The existence of these multiple subsets also calls into question the accepted paradigm of chromatin in establishment of latency. Exactly why I did not detect any changes in histone acetylation are not clear, but my data suggests that initial proviral repression may recruit other host factors, resulting in an entrenched network of chromatin-modifying factors and other repressive complexes. Histone acetylation, then, may be a marker for specific subsets of latently infected cells and not the entire reservoir.

This may explain the discrepancy between the importance of histone acetylation in cell line models and the complete absence of any evidence that histone deacetylase inhibitors can perturb the viral reservoir *in vivo*. However, evidence exists that a cocktail of LRAs including HDACi's result in greater viral reactivation than a single drug, perhaps through interruption of multiple arms of whatever repressive transcriptional network eventually maintains a silent provirus in its latent state.

Regardless, no clinical drug may be capable of clearing the entire viral reservoir. Instead, based on my data indicating that multiple forms of latency exist, I propose that a functional cure may be achieved through treatments that bias infected cells towards deep-seated latency. Virus integrated into cells with the low-affinity chimeric antigen receptors was not easily responsive to PMA or antibodies against the endogenous CD3 and CD28 receptors, which are significantly stronger than any cocktail which may be brought into clinic. It is reasonable to assume then that no biological effect may achieve a greater level of stimulation either. Antigen presentation in the context of an antigen-presenting cell may provide multiple signals but it is unlikely that this interaction would persist for a full day, as in an *in vitro* anti-CD3/CD28 condition. These infected cells then might pose no direct harm to the host, although they may re-seed the latent reservoir through clonal proliferation.

Remaining Mechanistic Questions

My work does not address all suggested mechanisms that contribute to latency such as host integration site, proviral genomic integrity, and transcriptional interference from neighboring genes. Regarding polymerase interference, evidence from our lab has shown that RNAPII read-through from the host promoter contributes little to HIV-1 transcriptional regulation. Through analysis of multiple cell lines with integrated proviruses in differing orientation to the host gene, no differences could be detected in latency reversal (Kaczmarek Michaels *et al.*, 2015). However, binding of NELF appeared

to be the primary regulatory factor in all conditions, in agreement with the evidence presented in Chapter Three. Future work on this project should consist of genomic sequencing to determine if I am polarizing integration sites towards or away from heterochromatic regions under low activation conditions and further PCR analysis to verify the integration of the viral genome, similar to that outlined by the Siliciano group (Bruner *et al.*, 2016).

The Impact of TCR Signaling on T Cell Function and Differentiation

In an effort to verify that signaling through the chimeric antigen receptors recapitulated endogenous TCR signaling cascades, I analyzed the phenotypes of differentially stimulated CD4+ T cells in multiple experiments including a microarray and flow analysis of surface markers. In addition to validating the CAR system, these assays raise a number of intriguing questions regarding the impact of signal strength on T cell function. As can be seen in the microarray analysis in Figure 3.2, multiple genes are immediately induced or repressed upon the slightest level of cellular stimulation. These genes, including the transcription factor KLF10, appear to require a low signaling threshold in order to become expressed. Other genes, including IL2, are transcribed in a gradient fashion and directly correlated to the level of upstream activation. Finally, a subset of genes exists, including FOXP3, a differentiation marker for Tregs (Allan *et al.*, 2005), that is induced by robust signaling, only achieved through engagement of the endogenous receptor (Table 3.1).

Instead of the creation of distinct T cell subsets in which all cells that express the same surface antigens have similar gene profiles, our data suggest that there may be a functional spectrum regardless of T cell phenotype. A range of transcriptional activity can exist within the same cell subsets due to varying signaling thresholds that may or may not have been reached. TCR stimulation uniformly results in an expansion of the CCR7+ CD45RA- population (Figure 3.4), often indicative of central memory cells (Okada *et al.*, 2008). However, the expression of most gene transcripts in Figure 3.2 are distinctly different between cells stimulated through the low affinity CAR and those activated by antibodies to CD3 and CD28. The impact of signaling on T cell cytokine production, further differentiation, and other functional outcomes within these memory populations may be considerable.

Some of the genes most differentially regulated upon TCR stimulation in Figure 3.2 and Table A.1 (see Appendix) are those involved in either DNA replication, such as the nuclease RNASEH1 and the replication protein RPA3, or metabolism, including the glycolysis enzymes ENO1 and PGK1. The metabolic profiles of T cell subsets and their role within the immune response are of significant interest. For instance, a recent study identified glycolysis-related gene networks as critical to the capacity of T_h17 cells to differentiate into T_h1 cells (Karmaus *et al.*, 2019). Further, it has been shown that the capacity of the host cell to conduct glycolysis is a key regulator of HIV-1 replication (Hegedus, Kavanagh Williamson and Huthoff, 2014) and may itself be increased upon viral infection (Hollenbaugh, Munger and Kim, 2011). My experiments highlight the importance of T cell signaling on both HIV-1 replication and cellular differentiation.

Study Limitations

While the research contained within this dissertation highlights several key mechanisms which regulate latent HIV-1, the findings presented here are in no way intended to be a complete summary of all factors which bias the balance between inducible and non-inducible latent reservoirs. I have thoroughly discussed the impact of signal amplitude on HIV-1 expression, but I have not analyzed signal quality. Future experiments within the Henderson lab will include the mutations of key residues within the CD28 and CD3ζ signaling domains of the chimeric antigen receptors in order to determine which residues and more importantly which signaling cascades are critical for the increase in HIV-1 expression that is observed upon TCR engagement.

In addition, work done by a fellow graduate student, Kyle Pedro, has indicated that HIV-1 infections in the context of an immunological synapse between a CD4+ T cell and a dendritic cell can compensate for suboptimal signaling within the target cell. The exact nature of these compensatory signals, and if inhibitory signals from receptors such as CTLA-4, PD-1, and Tim-3 also modulate the TCR-HIV axis, is not explored here.

I have also not described the nature of timing on HIV-1 infection. It is known that T cell activation prior to viral entry facilitates robust HIV-1 replication; however, the role of weak T cell signaling at this time point has not been fully examined. Minimal cellular activation prior to HIV-1 fusion with the cell membrane may allow for the expression of necessary entry receptors without providing an optimal environment for reverse transcription of the viral RNA genome or transcription of the integrated provirus. For

instance, the Lewin model of HIV-1 latency manipulates cells via treatment with CCL19 and CCL21, which renders them susceptible to HIV-1 integration but is not sufficient for subsequent transcription (Saleh *et al.*, 2007). The fact that the CCL19 receptor CCR7 regulates HIV-1 integration via NF-κB induction (Saleh *et al.*, 2016), but that this is inadequate for NF-κB - mediated transcription, provides more evidence for our conclusions regarding the existence of signaling thresholds that control HIV-1 expression. In contrast to the effects of CCR7 ligands, culturing CD4+ T cells with IL-7 prior to infection has been shown to provide the necessary stimulation for efficient HIV-1 replication (Steffens *et al.*, 2002), while IL-27 restricts HIV-1 expression in PBMCs (Fakruddin *et al.*, 2007). The level of cellular activation prior to viral entry, and the exact quantity and quality of signaling cascades involved, should be explored in further studies.

My experiments focused on the impact of T cell receptor signaling at the time of infection on HIV-1 expression and latency reversal and revealed that this effect persisted for at least one week. However, latency in the context of a HIV+ individual may persist for the entire lifespan of an infected cell. With further optimization of our tunable model to extend the time of survival of CAR+ primary CD4+ T cells after HIV-1 infection, the Henderson lab will be able to address questions about the dynamics of latency reversal.

In addition, I have not discussed the mechanisms that contribute to HIV-1 latency in other cellular reservoirs. In Chapter One, I discussed the contributions of γδ T cells and macrophages to HIV-1 persistence. Although evidence exists that establishment and maintenance of HIV-1 latency may require cell-specific factors, I do not address that here. For instance, HIV-1 inhibits apoptosis within infected macrophages by upregulating

the cell survival receptor TREM-1 or Triggering receptor expressed on myeloid cells-1 (Yuan *et al.*, 2017). This is a cell-specific mechanism, which relies upon signals downstream from TREM-1 to establish latency. The Cannon lab also identified the CoREST complex (Corepressor to RE1 silencing transcription factor) as a microglia-specific inhibitor of HIV-1 transcription in humanized mice. Because this is a unique mechanism for silencing of HIV-1 expression, microglia cells are especially responsive to LRAs that disrupt the CoREST complex (Llewellyn *et al.*, 2018). However, my experiments highlight the establishment of HIV-1 latency in CD4+ T cells and the LRAs that may disrupt viral repression in those cells. Future cure efforts will require both the manipulation of the balance between inducible and non-inducible latent CD4+ T cell subsets as well as strategies to target HIV-1 persistence in other cell types.

In regards to the use of nuclease-deficient Cas9-KRAB, I have only presented preliminary data here. I have not described a method of delivery or analyzed any off-target effects. Our lab is currently conducting experiments using multiple forms of latency reversing agents, and our eventual goal is to examine KRAB-Kap1 repression of HIV-1 in primary CD4+ T cells. KRAB-Kap1 is a promising complex for manipulating HIV-1 proviral expression. If we can better understand the function of other cellular host factors, additional key transcription factors might be utilized in a cell-specific manner.

Clinical Implications

A functional cure of HIV-1 would have profound benefits to those living with HIV/AIDS. In spite of all of the progress obtained since the height of the epidemic in the 1980's, a significant portion of the population remains at risk of contracting HIV-1 and living with lifelong immune dysfunction. Challenges at producing a broad-spectrum vaccine or at achieving a clinically viable cure using gene excision remain daunting. Instead, a functional cure, in which a patient can cease antiretroviral therapy for years or decades with only occasional follow-up, represents the gold standard of HIV-1 therapy going forward.

The existence of at least two latent reservoirs, one which is readily inducible to the strongest LRAs *ex vivo* and one which remains refractory to stimulation after multiple challenges (Hosmane *et al.*, 2017), suggests that a complete reversal of all potentially inducible latent proviruses may not be feasible. Instead, I present here the possibility of achieving permanent epigenetic silencing of all integrated HIV-1. Since cellular mechanisms that are recruited at the time of infection have long-term consequences on viral fate, there may be a therapeutic window in which to bias the balance between these two latent populations. My work also suggests that a two-step approach may be required: a cocktail of LRAs taken shortly after infection to remove the most easily reversible proviruses and then a gene editing based technique to further suppress all remaining infections into a deep-seated latency.

The viral reservoir after years of suppressive therapy will not resemble the original population of infected cells. Differences in clonal proliferation and changes to epigenetic marks may alter the chromatin environment so that it no longer mimics the layers of repression observed in the original infected ancestor cells (Zerihun *et al.*, 2015; Wang *et al.*, 2018). However, the ability of KRAB-Kap1 mediated repression to persist despite cellular division (Ayyanathan *et al.*, 2003) suggests that some of the epigenetic changes which occur during a new round of viral infection today may dictate the nature and dynamics of the latent reservoir for the remaining decades of a patient's life. While this poses serious challenges, the research conducted for this dissertation suggests that we may also be able to shape the future latent reservoir in a beneficial manner for the patient.

APPENDIX: MICROARRAY ANALYIS OF DIFFERENTIALLY STIMULATED CD4+ T CELLS IN CHAPTER THREE

Principal Component Analysis

Principal component analysis was performed on the genes listed as significantly different from the baseline unstimulated CD4+ T cell condition in the microarray shown for Figure 3.2. The separation of samples by treatment along the PC1 axis explains 29% of all variance, while PC2 explains 16% of all variance (Figure A.1). Clear clustering can be seen between all experimental conditions, with the low and high affinity CAR-expressing cells appearing intermediate between the unstimulated and TCR-stimulated groups.

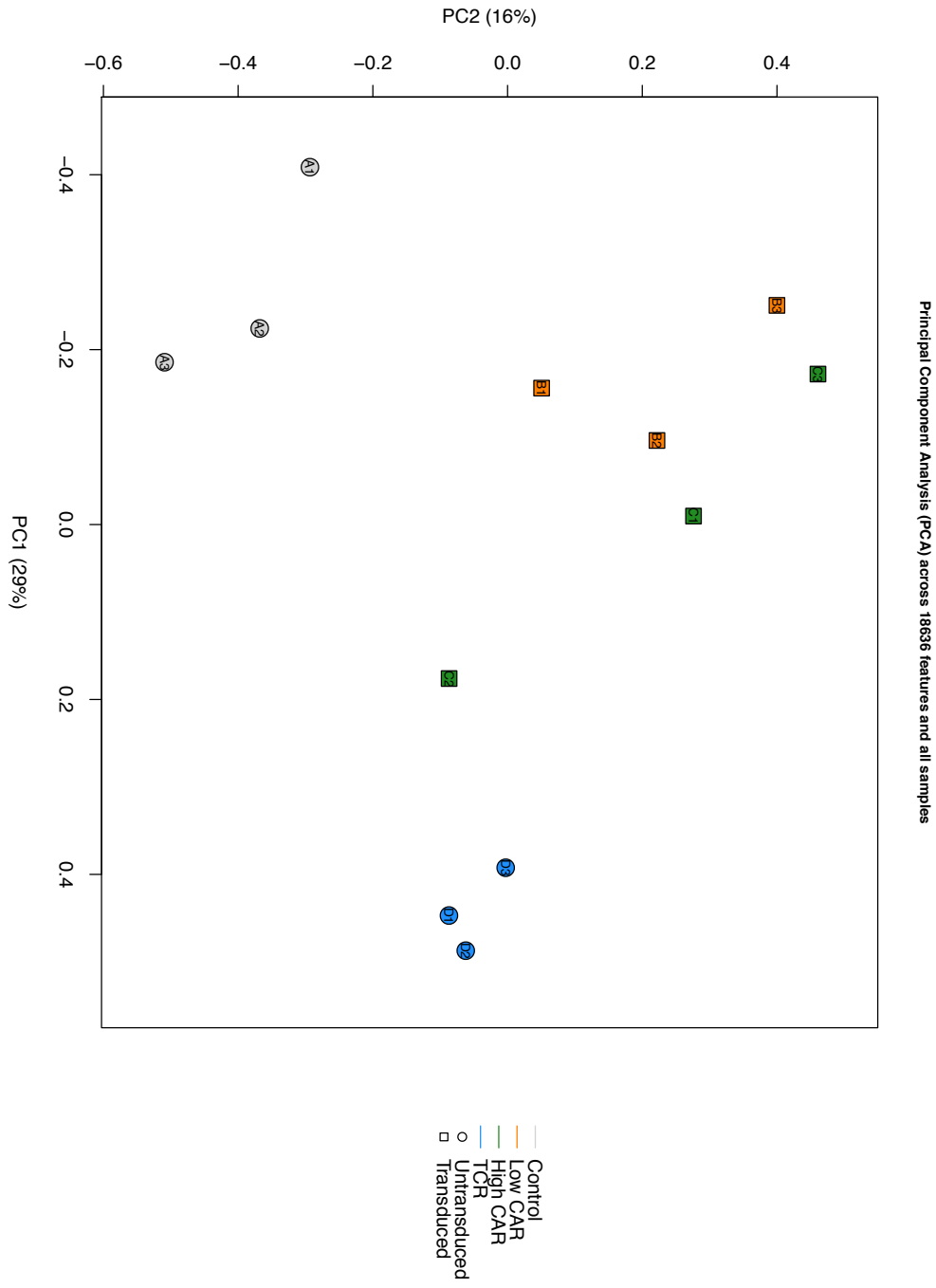


Figure A.1: Magnitude of T cell signaling differentially regulates genes in a gradient fashion. Signaling from the low affinity and high affinity CAR display an intermediate phenotype between that of the unstimulated and TCR-stimulated conditions. Principal component analysis was performed on all genes listed as significantly differentially expressed between conditions. The percentage of variance across all conditions explained by each principal component axis is listed as a percentage. See also Figure 3.2.

Microarray Analysis

All genes shown in the microarray in Figure 3.2, each of which has a one-way Anova FDR-corrected *q* value of less than 0.01. Each gene is listed along with its Human Entrez Gene ID, accepted description, and cluster number.

Table A.1: List of genes whose expression is significantly altered upon TCR stimulation. All genes from the microarray listed in Figure 3.2 are described in the following pages. Genes were arbitrarily assigned to clusters based on gene expression patterns.

Human Entrez Gene ID(s)	Symbol	Description	Cluster
10952	SEC61B	Sec61 translocon beta subunit	1
51114	ZDHHC9	zinc finger DHHC-type containing 9	1
115098	CCDC124	coiled-coil domain containing 124	1
64118	DUS1L	dihydrouridine synthase 1 like	1
79644	SRD5A3	steroid 5 alpha-reductase 3	1
9643	MORF4L2	mortality factor 4 like 2	1
1802	DPH2	DPH2 homolog	1
150223	YDJC	YdjC homolog (bacterial)	1
54998	AURKAIP1	aurora kinase A interacting protein 1	1
7277	TUBA4A	tubulin alpha 4a	1
55004	LAMTOR1	late endosomal/lysosomal adaptor, MAPK and MTOR activator 1	1
8321	FZD1	frizzled class receptor 1	1
4074	M6PR	mannose-6-phosphate receptor, cation dependent	1
2720	GLB1	galactosidase beta 1	1
7469	NELFA	negative elongation factor complex member A	1
60496	AASDHPPT	aminoadipate-semialdehyde dehydrogenase-phosphopantetheinyl transferase	1
5479	PPIB	peptidylprolyl isomerase B	1
84337	ELOF1	elongation factor 1 homolog	1
27314	RAB30	RAB30, member RAS oncogene family	1
27247	NFU1	NFU1 iron-sulfur cluster scaffold	1
157922	CAMSAP1	calmodulin regulated spectrin associated protein 1	1
51629	SLC25A39	solute carrier family 25 member 39	1
64769	MEAF6	MYST/Esa1 associated factor 6	1
29081	METTL5	methyltransferase like 5	1
58527	ABRACL	ABRA C-terminal like	1
11315	PARK7	Parkinsonism associated deglycase	1
1233	CCR4	C-C motif chemokine receptor 4	1
4726	NDUFS6	NADH:ubiquinone oxidoreductase subunit S6	1
6346	CCL1	C-C motif chemokine ligand 1	1
28974	C19orf53	chromosome 19 open reading frame 53	1
10286	BCAS2	breast carcinoma amplified sequence 2	1
5133	PDCD1	programmed cell death 1	1
6846	XCL2	X-C motif chemokine ligand 2	1
6375	XCL1	X-C motif chemokine ligand 1	1
11043	MID2	midline 2	1
83443	SF3B5	splicing factor 3b subunit 5	1
9764	KIAA0513	KIAA0513	1
4697	NDUFA4	NDUFA4, mitochondrial complex associated	1
55852	TEX2	testis expressed 2	1
5777	PTPN6	protein tyrosine phosphatase, non-receptor type 6	1
5325	PLAGL1	PLAG1 like zinc finger 1	1
928	CD9	CD9 molecule	1
10897	YIF1A	Yip1 interacting factor homolog A, membrane trafficking protein	1

26090	ABHD12	abhydrolase domain containing 12	1
89927	C16orf45	chromosome 16 open reading frame 45	1
8600	TNFSF11	tumor necrosis factor superfamily member 11	1
3394	IRF8	interferon regulatory factor 8	1
5606	MAP2K3	mitogen-activated protein kinase kinase 3	1
2539	G6PD	glucose-6-phosphate dehydrogenase	1
7074	TIAM1	T-cell lymphoma invasion and metastasis 1	1
518	ATP5G3	ATP synthase, H+ transporting, mitochondrial Fo complex subunit C3 (subunit 9)	1
3732	CD82	CD82 molecule	1
619279	ZNF704	zinc finger protein 704	1
51406	NOL7	nucleolar protein 7	1
6500	SKP1	S-phase kinase associated protein 1	1
1020	CDK5	cyclin dependent kinase 5	1
2787	GNG5	G protein subunit gamma 5	1
91582	RPS19BP1	ribosomal protein S19 binding protein 1	1
200894	ARL13B	ADP ribosylation factor like GTPase 13B	1
6367	CCL22	C-C motif chemokine ligand 22	1
55630	SLC39A4	solute carrier family 39 member 4	1
3682	ITGAE	integrin subunit alpha E	1
2589	GALNT1	polypeptide N-acetylgalactosaminyltransferase 1	1
22906	TRAK1	trafficking kinesin protein 1	1
9562	MINPP1	multiple inositol-polyphosphate phosphatase 1	1
5875	RABGGTA	Rab geranylgeranyltransferase alpha subunit	1
2182	ACSL4	acyl-CoA synthetase long-chain family member 4	1
5997	RGS2	regulator of G-protein signaling 2	1
5066	PAM	peptidylglycine alpha-amidating monooxygenase	1
51096	UTP18	UTP18, small subunit processome component	1
51726	DNAJB11	DnaJ heat shock protein family (Hsp40) member B11	1
3320	HSP90AA1	heat shock protein 90 alpha family class A member 1	1
54438	GFOD1	glucose-fructose oxidoreductase domain containing 1	1
5569	PKIA	protein kinase (cAMP-dependent, catalytic) inhibitor alpha	1
90441	ZNF622	zinc finger protein 622	1
7133	TNFRSF1B	TNF receptor superfamily member 1B	1
27333	GOLIM4	golgi integral membrane protein 4	1
134637	ADAT2	adenosine deaminase, tRNA specific 2	1
7150	TOP1	topoisomerase (DNA) I	1
10915	TCERG1	transcription elongation regulator 1	1
811	CALR	calreticulin	1
8425	LTBP4	latent transforming growth factor beta binding protein 4	1
5450	POU2AF1	POU class 2 associating factor 1	1
56253	CRTAM	cytotoxic and regulatory T-cell molecule	1
23305	ACSL6	acyl-CoA synthetase long-chain family member 6	1
57472	CNOT6	CCR4-NOT transcription complex subunit 6	1
58526	MID1IP1	MID1 interacting protein 1	1
11057	ABHD2	abhydrolase domain containing 2	1
25822	DNAJB5	DnaJ heat shock protein family (Hsp40) member B5	1
9882	TBC1D4	TBC1 domain family member 4	1
58493	INIP	INTS3 and NABP interacting protein	1
4023	LPL	lipoprotein lipase	1
79929	MAP6D1	MAP6 domain containing 1	1
3904	LAIR2	leukocyte associated immunoglobulin like receptor 2	1
11098	PRSS23	protease, serine 23	1
23012	STK38L	serine/threonine kinase 38 like	1
11022	TDRKH	tudor and KH domain containing	1
4151	MB	myoglobin	1
26090	ABHD12	abhydrolase domain containing 13	1
89927	C16orf45	chromosome 16 open reading frame 46	1
8600	TNFSF11	tumor necrosis factor superfamily member 12	1
3394	IRF8	interferon regulatory factor 9	1
5606	MAP2K3	mitogen-activated protein kinase kinase 4	1
2539	G6PD	glucose-6-phosphate dehydrogenase	1
7074	TIAM1	T-cell lymphoma invasion and metastasis 2	1
518	ATP5G3	ATP synthase, H+ transporting, mitochondrial Fo complex subunit C3 (subunit 9)	1
3732	CD82	CD82 molecule	1
619279	ZNF704	zinc finger protein 705	1

5683	PSMA2	proteasome subunit alpha 2	1
5689	PSMB1	proteasome subunit beta 1	1
10808	HSPH1	heat shock protein family H (Hsp110) member 1	1
3274	HRH2	histamine receptor H2	1
10128	LRPPRC	leucine rich pentatricopeptide repeat containing	1
1718	DHCR24	24-dehydrocholesterol reductase	1
84679	SLC9A7	solute carrier family 9 member A7	1
80185	TTI2	TELO2 interacting protein 2	1
84890	ADO	2-aminoethanethiol dioxygenase	1
388753	COA6	cytochrome c oxidase assembly factor 6	1
8140	SLC7A5	solute carrier family 7 member 5	1
55486	PARL	presenilin associated rhomboid like	1
7415	VCP	valosin containing protein	1
2180	ACSL1	acyl-CoA synthetase long-chain family member 1	1
7803	PTP4A1	protein tyrosine phosphatase type IVA, member 1	1
29107	NXT1	nuclear transport factor 2 like export factor 1	1
53615	MBD3	methyl-CpG binding domain protein 3	1
84328	LZIC	leucine zipper and CTNNBIP1 domain containing	1
51428	DDX41	DEAD-box helicase 41	1
150678	COPS9	COP9 signalosome subunit 9	1
54915	YTHDF1	YTH N6-methyladenosine RNA binding protein 1	1
1368	CPM	carboxypeptidase M	1
7128	TNFAIP3	TNF alpha induced protein 3	1
81570	CLPB	ClpB homolog, mitochondrial AAA ATPase chaperonin	1
7071	KLF10	Kruppel like factor 10	1
3725	JUN	Jun proto-oncogene, AP-1 transcription factor subunit	1
22827	PUF60	poly(U) binding splicing factor 60	1
54733	SLC35F2	solute carrier family 35 member F2	1
2153	F5	coagulation factor V	1
3516	RBPJ	recombination signal binding protein for immunoglobulin kappa J region	1
7203	CCT3	chaperonin containing TCP1 subunit 3	1
4869	NPM1	nucleophosmin	1
22948	CCT5	chaperonin containing TCP1 subunit 5	1
54888	NSUN2	NOP2/Sun RNA methyltransferase family member 2	1
11001	SLC27A2	solute carrier family 27 member 2	1
11169	WDHD1	WD repeat and HMG-box DNA binding protein 1	1
2107	ETF1	eukaryotic translation termination factor 1	1
8568	RRP1	ribosomal RNA processing 1	1
2023	ENO1	enolase 1	1
50628	GEMIN4	gem nuclear organelle associated protein 4	1
9322	TRIP10	thyroid hormone receptor interactor 10	1
84295	PHF6	PHD finger protein 6	1
9939	RBM8A	RNA binding motif protein 8A	1
55605	KIF21A	kinesin family member 21A	1
1173	AP2M1	adaptor related protein complex 2 mu 1 subunit	1
9618	TRAF4	TNF receptor associated factor 4	1
10098	TSPAN5	tetraspanin 5	1
23246	BOP1	block of proliferation 1	1
6385	SDC4	syndecan 4	1
908	CCT6A	chaperonin containing TCP1 subunit 6A	1
54206	ERRFI1	ERBB receptor feedback inhibitor 1	1
28984	RGCC	regulator of cell cycle	1
5315	PKM	pyruvate kinase, muscle	1
402055	SRRD	SRR1 domain containing	1
3028	HSD17B10	hydroxysteroid 17-beta dehydrogenase 10	1
10783	NEK6	NIMA related kinase 6	1
26521	TIMM8B	translocase of inner mitochondrial membrane 8 homolog B	1
10067	SCAMP3	secretory carrier membrane protein 3	1
4706	NDUFAB1	NADH:ubiquinone oxidoreductase subunit AB1	1
10514	MYBBP1A	MYB binding protein 1a	1
10541	ANP32B	acidic nuclear phosphoprotein 32 family member B	1
27044	SND1	staphylococcal nuclease and tudor domain containing 1	1
4121	MAN1A1	mannosidase alpha class 1A member 1	1
3945	LDHB	lactate dehydrogenase B	1
84946	LTV1	LTV1 ribosome biogenesis factor	1

9456	HOMER1	homer scaffolding protein 1	1
80896	NPL	N-acetylneuraminate pyruvate lyase	1
1026	CDKN1A	cyclin dependent kinase inhibitor 1A	1
50615	IL21R	interleukin 21 receptor	1
83858	ATAD3B	ATPase family, AAA domain containing 3B	1
3326	HSP90AB1	heat shock protein 90 alpha family class B member 1	1
1493	CTLA4	cytotoxic T-lymphocyte associated protein 4	1
8444	DYRK3	dual specificity tyrosine phosphorylation regulated kinase 3	1
23135	KDM6B	lysine demethylase 6B	1
23223	RRP12	ribosomal RNA processing 12 homolog	1
25902	MTHFD1L	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1-like	1
22856	CHSY1	chondroitin sulfate synthase 1	1
85458	DIXDC1	DIX domain containing 1	1
817	CAMK2D	calcium/calmodulin dependent protein kinase II delta	1
10252	SPRY1	sprouty RTK signaling antagonist 1	1
25911	DPCD	deleted in primary ciliary dyskinesia homolog (mouse)	1
219	ALDH1B1	aldehyde dehydrogenase 1 family member B1	1
57213	SPRYD7	SPRY domain containing 7	1
10171	RCL1	RNA terminal phosphate cyclase like 1	1
5516	PPP2CB	protein phosphatase 2 catalytic subunit beta	1
25929	GEMIN5	gem nuclear organelle associated protein 5	1
55161	TMEM33	transmembrane protein 33	1
25778	DSTYK	dual serine/threonine and tyrosine protein kinase	1
11338	U2AF2	U2 small nuclear RNA auxiliary factor 2	1
283871	PGP	phosphoglycolate phosphatase	1
8884	SLC5A6	solute carrier family 5 member 6	1
79586	CHPF	chondroitin polymerizing factor	1
283373	ANKRD52	ankyrin repeat domain 52	1
55319	TMA16	translation machinery associated 16 homolog	1
55269	PSPC1	paraspeckle component 1	1
7511	XPNPEP1	X-prolyl aminopeptidase 1	1
1836	SLC26A2	solute carrier family 26 member 2	1
113251	LARP4	La ribonucleoprotein domain family member 4	1
9656	MDC1	mediator of DNA damage checkpoint 1	1
254428	SLC41A1	solute carrier family 41 member 1	1
8161	COIL	coilin	1
65059	RAPH1	Ras association (RalGDS/AF-6) and pleckstrin homology domains 1	1
8807	IL18RAP	interleukin 18 receptor accessory protein	1
10018	BCL2L11	BCL2 like 11	1
2597	GAPDH	glyceraldehyde-3-phosphate dehydrogenase	1
6907	TBL1X	transducin beta like 1X-linked	1
9047	SH2D2A	SH2 domain containing 2A	1
64759	TNS3	tensin 3	1
200734	SPRED2	sprouty related EVH1 domain containing 2	1
6050	RNH1	ribonuclease/angiogenin inhibitor 1	1
1390	CREM	cAMP responsive element modulator	1
4810	NHS	NHS actin remodeling regulator	1
969	CD69	CD69 molecule	1
597	BCL2A1	BCL2 related protein A1	1
1293	COL6A3	collagen type VI alpha 3 chain	1
64218	SEMA4A	semaphorin 4A	1
8464	SUPT3H	SPT3 homolog, SAGA and STAGA complex component	1
3557	IL1RN	interleukin 1 receptor antagonist	1
6319	SCD	stearoyl-CoA desaturase	1
10849	CD3EAP	CD3e molecule associated protein	1
50	ACO2	aconitase 2	1
160760	PPTC7	PTC7 protein phosphatase homolog	1
51255	RNF181	ring finger protein 181	1
90378	SAMD1	sterile alpha motif domain containing 1	1
191	AHCY	adenosylhomocysteinase	1
9446	GSTO1	glutathione S-transferase omega 1	1
6780	STAU1	staufen double-stranded RNA binding protein 1	1
9112	MTA1	metastasis associated 1	1
2885	GRB2	growth factor receptor bound protein 2	1
4642	MYO1D	myosin ID	1

10273	STUB1	STIP1 homology and U-box containing protein 1	1
64651	CSRNP1	cysteine and serine rich nuclear protein 1	1
22822	PHLDA1	pleckstrin homology like domain family A member 1	1
8566	PDXK	pyridoxal (pyridoxine, vitamin B6) kinase	1
8482	SEMA7A	semaphorin 7A (John Milton Hagen blood group)	1
7421	VDR	vitamin D (1,25- dihydroxyvitamin D3) receptor	1
59269	HIVEP3	human immunodeficiency virus type I enhancer binding protein 3	1
54602	NDFIP2	Nedd4 family interacting protein 2	1
1958	EGR1	early growth response 1	1
1846	DUSP4	dual specificity phosphatase 4	1
1959	EGR2	early growth response 2	1
135228	CD109	CD109 molecule	1
8013	NR4A3	nuclear receptor subfamily 4 group A member 3	1
4345	CD200	CD200 molecule	1
3604	TNFRSF9	TNF receptor superfamily member 9	1
51320	MEX3C	mex-3 RNA binding family member C	1
9645	MICAL2	microtubule associated monooxygenase, calponin and LIM domain containing 2	1
5738	PTGFRN	prostaglandin F2 receptor inhibitor	1
6004	RGS16	regulator of G-protein signaling 16	1
9669	EIF5B	eukaryotic translation initiation factor 5B	1
3662	IRF4	interferon regulatory factor 4	1
57109	REXO4	REX4 homolog, 3'-5' exonuclease	1
79814	AGMAT	agmatinase	1
55544	RBM38	RNA binding motif protein 38	1
9904	RBM19	RNA binding motif protein 19	1
10488	CREB3	cAMP responsive element binding protein 3	1
4791	NFKB2	nuclear factor kappa B subunit 2	1
54874	FNBP1L	formin binding protein 1 like	1
55640	FLVCR2	feline leukemia virus subgroup C cellular receptor family member 2	1
9513	FXR2	FMR1 autosomal homolog 2	1
29979	UBQLN1	ubiquilin 1	1
55341	LSG1	large 60S subunit nuclear export GTPase 1	1
9987	HNRNPDL	heterogeneous nuclear ribonucleoprotein D like	1
3783	KCNN4	potassium calcium-activated channel subfamily N member 4	1
6520	SLC3A2	solute carrier family 3 member 2	1
26574	AATF	apoptosis antagonizing transcription factor	1
56957	OTUD7B	OTU deubiquitinase 7B	1
65094	JMJD4	jumonji domain containing 4	1
56270	WDR45B	WD repeat domain 45B	1
5688	PSMA7	proteasome subunit alpha 7	1
51042	ZNF593	zinc finger protein 593	1
3727	JUND	JunD proto-oncogene, AP-1 transcription factor subunit	1
85437	ZCRB1	zinc finger CCHC-type and RNA binding motif containing 1	1
55813	UTP6	UTP6, small subunit processome component	1
90480	GADD45GIP1	GADD45G interacting protein 1	1
5831	PYCR1	pyrroline-5-carboxylate reductase 1	1
4643	MYO1E	myosin IE	1
1407	CRY1	cryptochrome circadian clock 1	1
1329	COX5B	cytochrome c oxidase subunit 5B	1
7915	ALDH5A1	aldehyde dehydrogenase 5 family member A1	1
51529	ANAPC11	anaphase promoting complex subunit 11	1
31	ACACA	acetyl-CoA carboxylase alpha	1
57568	SIPA1L2	signal induced proliferation associated 1 like 2	1
6599	SMARCC1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin subfamily c member 1	1
9486	CHST10	carbohydrate sulfotransferase 10	1
56938	ARNTL2	aryl hydrocarbon receptor nuclear translocator like 2	1
3192	HNRNPU	heterogeneous nuclear ribonucleoprotein U	1
23507	LRRC8B	leucine rich repeat containing 8 family member B	1
26031	OSBPL3	oxysterol binding protein like 3	1
7528	YY1	YY1 transcription factor	1
23429	RYBP	RING1 and YY1 binding protein	1
5591	PRKDC	protein kinase, DNA-activated, catalytic polypeptide	1
7525	YES1	YES proto-oncogene 1, Src family tyrosine kinase	1
8932	MBD2	methyl-CpG binding domain protein 2	1

4779	NFE2L1	nuclear factor, erythroid 2 like 1	1
3054	HCFC1	host cell factor C1	1
2194	FASN	fatty acid synthase	1
28964	GIT1	GIT ArfGAP 1	1
29886	SNX8	sorting nexin 8	1
10153	CEBPZ	CCAAT/enhancer binding protein zeta	1
79050	NOC4L	nucleolar complex associated 4 homolog	1
10400	PEMT	phosphatidylethanolamine N-methyltransferase	1
115353	LRRC42	leucine rich repeat containing 42	1
57478	USP31	ubiquitin specific peptidase 31	1
1459	CSNK2A2	casein kinase 2 alpha 2	1
282969	FUOM	fucose mutarotase	1
84320	ACBD6	acyl-CoA binding domain containing 6	1
56259	CTNNBL1	catenin beta like 1	1
254394	MCM9	minichromosome maintenance 9 homologous recombination repair factor	1
4884	NPTX1	neuronal pentraxin 1	1
10804	GJB6	gap junction protein beta 6	1
6617	SNAPC1	small nuclear RNA activating complex polypeptide 1	1
57584	ARHGAP21	Rho GTPase activating protein 21	1
4763	NF1	neurofibromin 1	1
7486	WRN	Werner syndrome RecQ like helicase	1
11325	DDX42	DEAD-box helicase 42	1
10975	UQCR11	ubiquinol-cytochrome c reductase, complex III subunit XI	1
5424	POLD1	DNA polymerase delta 1, catalytic subunit	1
9986	RCE1	Ras converting CAAX endopeptidase 1	1
90525	SHF	Src homology 2 domain containing F	1
55760	DHX32	DEAH-box helicase 32 (putative)	1
1263	PLK3	polo like kinase 3	1
8651	SOCS1	suppressor of cytokine signaling 1	1
54936	ADPRHL2	ADP-ribosylhydrolase like 2	1
5531	PPP4C	protein phosphatase 4 catalytic subunit	1
23640	HSPBP1	HSPA (Hsp70) binding protein 1	1
113000	RPUSD1	RNA pseudouridylate synthase domain containing 1	1
55527	FEM1A	fem-1 homolog A	1
1175	AP2S1	adaptor related protein complex 2 sigma 1 subunit	1
148022	TICAM1	toll like receptor adaptor molecule 1	1
55684	RABL6	RAB, member RAS oncogene family-like 6	1
8175	SF3A2	splicing factor 3a subunit 2	1
284106	CISD3	CDGSH iron sulfur domain 3	1
125988	C19orf70	chromosome 19 open reading frame 70	1
84134	TOMM40L	translocase of outer mitochondrial membrane 40 like	1
5094	PCBP2	poly(rC) binding protein 2	1
11140	CDC37	cell division cycle 37	1
2354	FOSB	FosB proto-oncogene, AP-1 transcription factor subunit	1
84216	TMEM117	transmembrane protein 117	1
677	ZFP36L1	ZFP36 ring finger protein like 1	1
7040	TGFB1	transforming growth factor beta 1	1
9265	CYTH3	cytohesin 3	1
80700	UBXN6	UBX domain protein 6	1
10048	RANBP9	RAN binding protein 9	1
3560	IL2RB	interleukin 2 receptor subunit beta	1
7763	ZFAND5	zinc finger AN1-type containing 5	1
9249	DHRS3	dehydrogenase/reductase 3	1
51564	HDAC7	histone deacetylase 7	1
92558	BICDL1	BICD family like cargo adaptor 1	1
26262	TSPAN17	tetraspanin 17	1
54985	HCFC1R1	host cell factor C1 regulator 1	1
923	CD6	CD6 molecule	1
10625	IVNS1ABP	influenza virus NS1A binding protein	1
57062	DDX24	DEAD-box helicase 24	1
22859	ADGRL1	adhesion G protein-coupled receptor L1	1
79169	C1orf35	chromosome 1 open reading frame 35	1
7057	THBS1	thrombospondin 1	1
1105	CHD1	chromodomain helicase DNA binding protein 1	1
113246	C12orf57	chromosome 12 open reading frame 57	1
6193	RPS5	ribosomal protein S5	1

353322	ANKRD37	ankyrin repeat domain 37	1
140823	ROMO1	reactive oxygen species modulator 1	1
401052	LOC401052	uncharacterized LOC401052	1
10948	STARD3	StAR related lipid transfer domain containing 3	1
80198	MUS81	MUS81 structure-specific endonuclease subunit	1
1855	DVL1	dishevelled segment polarity protein 1	1
3556	IL1RAP	interleukin 1 receptor accessory protein	1
4602	MYB	MYB proto-oncogene, transcription factor	1
8496	PPFIBP1	PPFIA binding protein 1	1
1960	EGR3	early growth response 3	1
3164	NR4A1	nuclear receptor subfamily 4 group A member 1	1
4862	NPAS2	neuronal PAS domain protein 2	1
2672	GFI1	growth factor independent 1 transcriptional repressor	1
5270	SERPINE2	serpin family E member 2	1
57190	SELENON	selenoprotein N	1
54815	GATAD2A	GATA zinc finger domain containing 2A	1
8270	LAGE3	L antigen family member 3	1
5524	PTPA	protein phosphatase 2 phosphatase activator	1
57688	ZSWIM6	zinc finger SWIM-type containing 6	1
51079	NDUFA13	NADH:ubiquinone oxidoreductase subunit A13	1
3720	JARID2	jumonji and AT-rich interaction domain containing 2	1
4851	NOTCH1	notch 1	1
23326	USP22	ubiquitin specific peptidase 22	1
6938	TCF12	transcription factor 12	1
9704	DHX34	DEAH-box helicase 34	1
26155	NOC2L	NOC2 like nucleolar associated transcriptional repressor	1
165	AEBP1	AE binding protein 1	1
115024	NT5C3B	5'-nucleotidase, cytosolic IIIB	1
10865	ARID5A	AT-rich interaction domain 5A	1
26051	PPP1R16B	protein phosphatase 1 regulatory subunit 16B	1
728489	DNLZ	DNL-type zinc finger	1
8761	PABPC4	poly(A) binding protein cytoplasmic 4	1
2768	GNA12	G protein subunit alpha 12	1
6633	SNRPD2	small nuclear ribonucleoprotein D2 polypeptide	1
7265	TTC1	tetratricopeptide repeat domain 1	1
2879	GPX4	glutathione peroxidase 4	1
59286	UBL5	ubiquitin like 5	1
5971	RELB	RELB proto-oncogene, NF-kB subunit	1
9092	SART1	squamous cell carcinoma antigen recognized by T-cells 1	1
23020	SNRNP200	small nuclear ribonucleoprotein U5 subunit 200	1
123169	LEO1	LEO1 homolog, Paf1/RNA polymerase II complex component	1
3995	FADS3	fatty acid desaturase 3	1
4298	MLLT1	MLLT1, super elongation complex subunit	1
54926	UBE2R2	ubiquitin conjugating enzyme E2 R2	1
3984	LIMK1	LIM domain kinase 1	1
5966	REL	REL proto-oncogene, NF-kB subunit	1
10451	VAV3	vav guanine nucleotide exchange factor 3	1
6713	SQLE	squalene epoxidase	1
3309	HSPA5	heat shock protein family A (Hsp70) member 5	1
79876	UBA5	ubiquitin like modifier activating enzyme 5	1
2534	FYN	FYN proto-oncogene, Src family tyrosine kinase	1
84524	ZC3H8	zinc finger CCCH-type containing 8	1
56937	PMEPA1	prostate transmembrane protein, androgen induced 1	1
7016	TESK1	testis-specific kinase 1	1
7185	TRAF1	TNF receptor associated factor 1	1
10746	MAP3K2	mitogen-activated protein kinase kinase kinase 2	1
51429	SNX9	sorting nexin 9	1
55342	STRBP	spermatid perinuclear RNA binding protein	1
56172	ANKH	ANKH inorganic pyrophosphate transport regulator	1
54880	BCOR	BCL6 corepressor	1
9766	SUSD6	sushi domain containing 6	1
6722	SRF	serum response factor	1
9603	NFE2L3	nuclear factor, erythroid 2 like 3	1
27161	AGO2	argonaute 2, RISC catalytic component	1
29954	POMT2	protein O-mannosyltransferase 2	1

8428	STK24	serine/threonine kinase 24	1
10072	DPP3	dipeptidyl peptidase 3	1
4282	MIF	macrophage migration inhibitory factor (glycosylation-inhibiting factor)	1
22876	INPP5F	inositol polyphosphate-5-phosphatase F	1
3399	ID3	inhibitor of DNA binding 3, HLH protein	1
26018	LRIG1	leucine rich repeats and immunoglobulin like domains 1	1
2275	FHL3	four and a half LIM domains 3	1
153020	RASGEF1B	RasGEF domain family member 1B	1
55589	BMP2K	BMP2 inducible kinase	1
23683	PRKD3	protein kinase D3	1
25797	QPCT	glutaminyl-peptide cyclotransferase	1
23541	SEC14L2	SEC14 like lipid binding 2	1
4929	NR4A2	nuclear receptor subfamily 4 group A member 2	1
55573	CDV3	CDV3 homolog	1
55353	LAPTM4B	lysosomal protein transmembrane 4 beta	1
5367	PMCH	pro-melanin concentrating hormone	1
9076	CLDN1	claudin 1	1
3267	AGFG1	ArfGAP with FG repeats 1	1
27076	LYPD3	LY6/PLAUR domain containing 3	1
521	ATP5I	ATP synthase, H+ transporting, mitochondrial Fo complex subunit E	1
1340	COX6B1	cytochrome c oxidase subunit 6B1	1
51700	CYB5R2	cytochrome b5 reductase 2	1
2118	ETV4	ETS variant 4	1
54935	DUSP23	dual specificity phosphatase 23	1
6168	RPL37A	ribosomal protein L37a	1
79763	ISOC2	isochorismatase domain containing 2	1
55621	TRMT1	tRNA methyltransferase 1	1
11267	SNF8	SNF8, ESCRT-II complex subunit	1
1347	COX7A2	cytochrome c oxidase subunit 7A2	1
79724	ZNF768	zinc finger protein 768	1
28955	DEXI	Dexi homolog	1
10555	AGPAT2	1-acylglycerol-3-phosphate O-acyltransferase 2	1
143903	LAYN	layilin	1
283209	PGM2L1	phosphoglucomutase 2 like 1	1
8507	ENC1	ectodermal-neural cortex 1	1
9749	PHACTR2	phosphatase and actin regulator 2	1
7390	UROS	uroporphyrinogen III synthase	1
84293	FAM213A	family with sequence similarity 213 member A	1
169792	GLIS3	GLIS family zinc finger 3	1
11019	LIAS	lipoic acid synthetase	1
9537	TP53I11	tumor protein p53 inducible protein 11	1
64092	SAMSN1	SAM domain, SH3 domain and nuclear localization signals 1	1
9398	CD101	CD101 molecule	1
128866	CHMP4B	charged multivesicular body protein 4B	1
914	CD2	CD2 molecule	1
56941	HMCES	5-hydroxymethylcytosine (hmC) binding, ES cell-specific	1
2744	GLS	glutaminase	1
481	ATP1B1	ATPase Na+/K+ transporting subunit beta 1	1
7832	BTG2	BTG anti-proliferation factor 2	1
121260	SLC15A4	solute carrier family 15 member 4	1
91647	ATPAF2	ATP synthase mitochondrial F1 complex assembly factor 2	1
11319	ECD	ecdysoneless cell cycle regulator	1
473	RERE	arginine-glutamic acid dipeptide repeats	1
6830	SUPT6H	SPT6 homolog, histone chaperone	1
10428	CFDP1	craniofacial development protein 1	1
2969	GTF2I	general transcription factor IIi	1
23396	PIP5K1C	phosphatidylinositol-4-phosphate 5-kinase type 1 gamma	1
220213	OTUD1	OTU deubiquitinase 1	1
5937	RBMS1	RNA binding motif single stranded interacting protein 1	1
60436	TGIF2	TGFB induced factor homeobox 2	1
4772	NFATC1	nuclear factor of activated T-cells 1	1
2026	ENO2	enolase 2	1
6774	STAT3	signal transducer and activator of transcription 3	1
80233	FAAP100	Fanconi anemia core complex associated protein 100	1
9859	CEP170	centrosomal protein 170	1

3091	HIF1A	hypoxia inducible factor 1 alpha subunit	1
26278	SACS	sacsin molecular chaperone	1
8202	NCOA3	nuclear receptor coactivator 3	1
4928	NUP98	nucleoporin 98	1
3446	IFNA10	interferon alpha 10	1
4637	MYL6	myosin light chain 6	1
51192	CKLF	chemokine like factor	1
11006	LILRB4	leukocyte immunoglobulin like receptor B4	1
29085	PHPT1	phosphohistidine phosphatase 1	1
10591	DNPH1	2'-deoxynucleoside 5'-phosphate N-hydrolase 1	1
8871	SYNJ2	synaptojanin 2	1
27151	CPAMD8	C3 and PZP like, alpha-2-macroglobulin domain containing 8	1
4122	MAN2A2	mannosidase alpha class 2A member 2	1
85450	ITPRIP	inositol 1,4,5-trisphosphate receptor interacting protein	1
115708	TRMT61A	tRNA methyltransferase 61A	1
119	ADD2	adducin 2	1
100506581	C16orf95	chromosome 16 open reading frame 95	1
25814	ATXN10	ataxin 10	1
2004	ELK3	ELK3, ETS transcription factor	1
23670	TMEM2	transmembrane protein 2	1
1119	CHKA	choline kinase alpha	1
51530	ZC3HC1	zinc finger C3HC-type containing 1	1
84865	CCDC142	coiled-coil domain containing 142	1
94104	PAXBP1	PAX3 and PAX7 binding protein 1	1
23138	N4BP3	NEDD4 binding protein 3	1
55128	TRIM68	tripartite motif containing 68	1
8505	PARG	poly(ADP-ribose) glycohydrolase	1
7343	UBTF	upstream binding transcription factor, RNA polymerase I	1
56970	ATXN7L3	ataxin 7 like 3	1
2314	FLII	FLII, actin remodeling protein	1
2622	GAS8	growth arrest specific 8	1
7090	TLE3	transducin like enhancer of split 3	1
64718	UNKL	unkempt family like zinc finger	1
284654	RSPO1	R-spondin 1	1
79171	RBM42	RNA binding motif protein 42	1
7874	USP7	ubiquitin specific peptidase 7	1
9757	KMT2B	lysine methyltransferase 2B	1
37	ACADVL	acyl-CoA dehydrogenase, very long chain	1
26279	PLA2G2D	phospholipase A2 group IID	1
4296	MAP3K11	mitogen-activated protein kinase kinase kinase 11	1
5739	PTGIR	prostaglandin I2 (prostacyclin) receptor (IP)	1
9058	SLC13A2	solute carrier family 13 member 2	1
79064	TMEM223	transmembrane protein 223	1
55206	SBNO1	strawberry notch homolog 1	1
24148	PRPF6	pre-mRNA processing factor 6	1
2535	FZD2	frizzled class receptor 2	1
7259	TSPYL1	TSPY like 1	1
8439	NSMAF	neutral sphingomyelinase activation associated factor	1
150946	GAREM2	GRB2 associated regulator of MAPK1 subtype 2	1
5213	PFKM	phosphofructokinase, muscle	2
6429	SRSF4	serine and arginine rich splicing factor 4	2
60481	ELOVL5	ELOVL fatty acid elongase 5	2
966	CD59	CD59 molecule	2
9276	COPB2	coatomer protein complex subunit beta 2	2
51386	EIF3L	eukaryotic translation initiation factor 3 subunit L	2
2072	ERCC4	ERCC excision repair 4, endonuclease catalytic subunit	2
4358	MPV17	MPV17, mitochondrial inner membrane protein	2
8655	DYNLL1	dynein light chain LC8-type 1	2
80219	COQ10B	coenzyme Q10B	2
8992	ATP6V0E1	ATPase H+ transporting V0 subunit e1	2
148203	ZNF738	zinc finger protein 738	2
93380	MMGT1	membrane magnesium transporter 1	2
51060	TXNDC12	thioredoxin domain containing 12	2
6539	SLC6A12	solute carrier family 6 member 12	2
388591	RNF207	ring finger protein 207	2

6727	SRP14	signal recognition particle 14	2
729852	UMAD1	UBAP1-MVB12-associated (UMA) domain containing 1	2
80381	CD276	CD276 molecule	2
84258	SYT3	synaptotagmin 3	2
23251	KIAA1024	KIAA1024	2
114836	SLAMF6	SLAM family member 6	2
6207	RPS13	ribosomal protein S13	2
728798	FRMPD2B	FERM and PDZ domain containing 2B, pseudogene	2
51759	C9orf78	chromosome 9 open reading frame 78	2
8837	CFLAR	CASP8 and FADD like apoptosis regulator	2
55012	PPP2R3C	protein phosphatase 2 regulatory subunit B''gamma	2
118426	BORCS5	BLOC-1 related complex subunit 5	2
8804	CREG1	cellular repressor of E1A stimulated genes 1	2
51008	ASCC1	activating signal cointegrator 1 complex subunit 1	2
142	PARP1	poly(ADP-ribose) polymerase 1	2
90355	C5orf30	chromosome 5 open reading frame 30	2
4802	NFYC	nuclear transcription factor Y subunit gamma	2
51188	SS18L2	SS18 like 2	2
84318	CCDC77	coiled-coil domain containing 77	2
133015	PACRGL	PARK2 coregulated like	2
79691	QTRT2	queuine tRNA-ribosyltransferase accessory subunit 2	2
10055	SAE1	SUMO1 activating enzyme subunit 1	2
8030	CCDC6	coiled-coil domain containing 6	2
3383	ICAM1	intercellular adhesion molecule 1	2
81691	LOC81691	exonuclease NEF-sp	2
90417	KNSTRN	kinetochore localized astrin/SPAG5 binding protein	2
7453	WARS	tryptophanyl-tRNA synthetase	2
9232	PTTG1	pituitary tumor-transforming 1	2
51155	HN1	hematological and neurological expressed 1	2
11244	ZHX1	zinc fingers and homeoboxes 1	2
6790	AURKA	aurora kinase A	2
7049	TGFBR3	transforming growth factor beta receptor 3	2
55165	CEP55	centrosomal protein 55	2
57405	SPC25	SPC25, NDC80 kinetochore complex component	2
221150	SKA3	spindle and kinetochore associated complex subunit 3	2
157570	ESCO2	establishment of sister chromatid cohesion N-acetyltransferase 2	2
9055	PRC1	protein regulator of cytokinesis 1	2
157313	CDCA2	cell division cycle associated 2	2
51433	ANAPC5	anaphase promoting complex subunit 5	2
83540	NUF2	NUF2, NDC80 kinetochore complex component	2
9738	CCP110	centriolar coiled-coil protein 110	2
11183	MAP4K5	mitogen-activated protein kinase kinase kinase kinase 5	2
22974	TPX2	TPX2, microtubule nucleation factor	2
10112	KIF20A	kinesin family member 20A	2
3161	HMMR	hyaluronan mediated motility receptor	2
79840	NHEJ1	non-homologous end joining factor 1	2
3148	HMGB2	high mobility group box 2	2
9787	DLGAP5	DLG associated protein 5	2
9212	AURKB	aurora kinase B	2
699	BUB1	BUB1 mitotic checkpoint serine/threonine kinase	2
11113	CIT	citron rho-interacting serine/threonine kinase	2
51203	NUSAP1	nucleolar and spindle associated protein 1	2
644	BLVRA	biliverdin reductase A	2
9928	KIF14	kinesin family member 14	2
7153	TOP2A	topoisomerase (DNA) II alpha	2
84548	TMEM185A	transmembrane protein 185A	2
54842	MFSD6	major facilitator superfamily domain containing 6	2
860	RUNX2	runt related transcription factor 2	2
8501	SLC43A1	solute carrier family 43 member 1	2
255231	MCOLN2	mucolipin 2	2
1326	MAP3K8	mitogen-activated protein kinase kinase kinase 8	2
4818	NKG7	natural killer cell granule protein 7	2
347734	SLC35B2	solute carrier family 35 member B2	2
2786	GNG4	G protein subunit gamma 4	2
6574	SLC20A1	solute carrier family 20 member 1	2

1889	ECE1	endothelin converting enzyme 1	2
54977	SLC25A38	solute carrier family 25 member 38	2
55362	TMEM63B	transmembrane protein 63B	2
81562	LMAN2L	lectin, mannose binding 2 like	2
55974	SLC50A1	solute carrier family 50 member 1	2
55432	YOD1	YOD1 deubiquitinase	2
64776	C11orf1	chromosome 11 open reading frame 1	2
92335	STRADA	STE20-related kinase adaptor alpha	2
5603	MAPK13	mitogen-activated protein kinase 13	2
85235	HIST1H2AH	histone cluster 1 H2A family member h	2
8360	HIST1H4D	histone cluster 1 H4 family member d	2
3017	HIST1H2BD	histone cluster 1 H2B family member d	2
8334	HIST1H2AC	histone cluster 1 H2A family member c	2
3007	HIST1H1D	histone cluster 1 H1 family member d	2
9447	AIM2	absent in melanoma 2	2
51510	CHMP5	charged multivesicular body protein 5	2
8969	HIST1H2AG	histone cluster 1 H2A family member g	2
8336	HIST1H2AM	histone cluster 1 H2A family member m	2
8339	HIST1H2BG	histone cluster 1 H2B family member g	2
8329	HIST1H2AI	histone cluster 1 H2A family member i	2
3012	HIST1H2AE	histone cluster 1 H2A family member e	2
55145	THAP1	THAP domain containing 1	2
55143	CDCA8	cell division cycle associated 8	2
1870	E2F2	E2F transcription factor 2	2
8365	HIST1H4H	histone cluster 1 H4 family member h	2
10682	EBP	emopamil binding protein (sterol isomerase)	2
51512	GTSE1	G2 and S-phase expressed 1	2
8331	HIST1H2AJ	histone cluster 1 H2A family member j	2
64792	IFT22	intraflagellar transport 22	2
8342	HIST1H2BM	histone cluster 1 H2B family member m	2
94120	SYTL3	synaptotagmin like 3	2
64782	AEN	apoptosis enhancing nuclease	2
64793	CEP85	centrosomal protein 85	2
4717	NDUFC1	NADH:ubiquinone oxidoreductase subunit C1	2
92815	HIST3H2A	histone cluster 3 H2A	2
291	SLC25A4	solute carrier family 25 member 4	2
10459	MAD2L2	MAD2 mitotic arrest deficient-like 2 (yeast)	2
9242	MSC	musculin	2
332	BIRC5	baculoviral IAP repeat containing 5	2
3835	KIF22	kinesin family member 22	2
1398	CRK	CRK proto-oncogene, adaptor protein	2
8367	HIST1H4E	histone cluster 1 H4 family member e	2
10945	KDELR1	KDEL endoplasmic reticulum protein retention receptor 1	2
79738	BBS10	Bardet-Biedl syndrome 10	2
63931	MRPS14	mitochondrial ribosomal protein S14	2
54987	C1orf123	chromosome 1 open reading frame 123	2
4090	SMAD5	SMAD family member 5	2
55831	EMC3	ER membrane protein complex subunit 3	2
255520	ELMOD2	ELMO domain containing 2	2
51128	SAR1B	secretion associated Ras related GTPase 1B	2
55140	ELP3	elongator acetyltransferase complex subunit 3	2
302	ANXA2	annexin A2	2
149420	PDIK1L	PDLIM1 interacting kinase 1 like	2
26586	CKAP2	cytoskeleton associated protein 2	2
135114	HINT3	histidine triad nucleotide binding protein 3	2
57102	C12orf4	chromosome 12 open reading frame 4	2
219790	RTKN2	rhotekin 2	2
80067	DCAF17	DDB1 and CUL4 associated factor 17	2
1654	DDX3X	DEAD-box helicase 3, X-linked	2
151188	ARL6IP6	ADP ribosylation factor like GTPase 6 interacting protein 6	2
10313	RTN3	reticulon 3	2
150468	CKAP2L	cytoskeleton associated protein 2 like	2
55182	RNF220	ring finger protein 220	2
9887	SMG7	SMG7, nonsense mediated mRNA decay factor	2
5579	PRKCB	protein kinase C beta	2

55435	AP1AR	adaptor related protein complex 1 associated regulatory protein	2
253635	GPATCH11	G-patch domain containing 11	2
55033	FKBP14	FK506 binding protein 14	2
5355	PLP2	proteolipid protein 2	2
51227	PIGP	phosphatidylinositol glycan anchor biosynthesis class P	2
11321	GPN1	GPN-loop GTPase 1	2
51573	GDE1	glycerophosphodiester phosphodiesterase 1	2
23786	BCL2L13	BCL2 like 13	2
6103	RPGR	retinitis pigmentosa GTPase regulator	2
26263	FBXO22	F-box protein 22	2
7163	TPD52	tumor protein D52	2
51068	NMD3	NMD3 ribosome export adaptor	2
51026	GOLT1B	golgi transport 1B	2
122809	SOCS4	suppressor of cytokine signaling 4	2
83695	RHNO1	RAD9-HUS1-RAD1 interacting nuclear orphan 1	2
26040	SETBP1	SET binding protein 1	2
5378	PMS1	PMS1 homolog 1, mismatch repair system component	2
10641	NPRL2	NPR2-like, GATOR1 complex subunit	2
84967	LSM10	LSM10, U7 small nuclear RNA associated	2
9702	CEP57	centrosomal protein 57	2
23062	GGA2	golgi associated, gamma adaptin ear containing, ARF binding protein 2	2
54780	NSMCE4A	NSE4 homolog A, SMC5-SMC6 complex component	2
199857	ALG14	ALG14, UDP-N-acetylglucosaminyltransferase subunit	2
28977	MRPL42	mitochondrial ribosomal protein L42	2
25996	REXO2	RNA exonuclease 2	2
3364	HUS1	HUS1 checkpoint clamp component	2
134359	POC5	POC5 centriolar protein	2
64778	FNDC3B	fibronectin type III domain containing 3B	2
256356	GK5	glycerol kinase 5 (putative)	2
9194	SLC16A7	solute carrier family 16 member 7	2
55037	PTCD3	pentatricopeptide repeat domain 3	2
8148	TAF15	TATA-box binding protein associated factor 15	2
285282	RABL3	RAB, member of RAS oncogene family like 3	2
51095	TRNT1	tRNA nucleotidyl transferase 1	2
8563	THOC5	THO complex 5	2
9317	PTER	phosphotriesterase related	2
1605	DAG1	dystroglycan 1	2
83939	EIF2A	eukaryotic translation initiation factor 2A	2
5877	RABIF	RAB interacting factor	2
10923	SUB1	SUB1 homolog, transcriptional regulator	2
387263	C6orf120	chromosome 6 open reading frame 120	2
28972	SPCS1	signal peptidase complex subunit 1	2
10463	SLC30A9	solute carrier family 30 member 9	2
1974	EIF4A2	eukaryotic translation initiation factor 4A2	2
6993	DYNLT1	dynein light chain Tctex-type 1	2
285331	CCDC66	coiled-coil domain containing 66	2
51691	LSM8	LSM8 homolog, U6 small nuclear RNA associated	2
84274	COQ5	coenzyme Q5, methyltransferase	2
9046	DOK2	docking protein 2	2
80824	DUSP16	dual specificity phosphatase 16	2
11186	RASSF1	Ras association domain family member 1	2
9524	TECR	trans-2,3-enoyl-CoA reductase	2
55909	BIN3	bridging integrator 3	2
953	ENTPD1	ectonucleoside triphosphate diphosphohydrolase 1	2
8530	CST7	cystatin F	2
11269	DDX19B	DEAD-box helicase 19B	2
8766	RAB11A	RAB11A, member RAS oncogene family	2
25977	NECAP1	NECAP endocytosis associated 1	2
2000	ELF4	E74 like ETS transcription factor 4	2
11040	PIM2	Pim-2 proto-oncogene, serine/threonine kinase	2
2585	GALK2	galactokinase 2	2
144402	CPNE8	copine 8	2
79139	DERL1	derlin 1	2
80196	RNF34	ring finger protein 34	2
11262	SP140	SP140 nuclear body protein	2

55312	RFK	riboflavin kinase	2
64854	USP46	ubiquitin specific peptidase 46	2
387882	C12orf75	chromosome 12 open reading frame 75	2
11270	NRM	nurim (nuclear envelope membrane protein)	2
896	CCND3	cyclin D3	2
143888	KDELC2	KDEL motif containing 2	2
5008	OSM	oncostatin M	2
10602	CDC42EP3	CDC42 effector protein 3	2
54918	CMTM6	CKLF like MARVEL transmembrane domain containing 6	2
1063	CENPF	centromere protein F	2
84243	ZDHHC18	zinc finger DHHC-type containing 18	2
382	ARF6	ADP ribosylation factor 6	2
134266	GRPEL2	GrpE like 2, mitochondrial	2
3001	GZMA	granzyme A	2
6352	CCL5	C-C motif chemokine ligand 5	2
55028	C17orf80	chromosome 17 open reading frame 80	2
23258	DENND5A	DENN domain containing 5A	2
56954	NIT2	nitrilase family member 2	2
93621	MRFAP1	Morf4 family associated protein 1	2
5347	PLK1	polo like kinase 1	2
58190	CTDSP1	CTD small phosphatase 1	2
2014	EMP3	epithelial membrane protein 3	2
5269	SERPINB6	serpin family B member 6	2
113802	HENMT1	HEN1 methyltransferase homolog 1	2
10578	GNLY	granulysin	2
5551	PRF1	perforin 1	2
26610	ELP4	elongator acetyltransferase complex subunit 4	2
9477	MED20	mediator complex subunit 20	2
8634	RTCA	RNA 3'-terminal phosphate cyclase	2
3428	IFI16	interferon gamma inducible protein 16	2
63901	FAM111A	family with sequence similarity 111 member A	2
55796	MBNL3	muscleblind like splicing regulator 3	2
2177	FANCD2	Fanconi anemia complementation group D2	3
86	ACTL6A	actin like 6A	3
57696	DDX55	DEAD-box helicase 55	3
54920	DUS2	dihydrouridine synthase 2	3
22809	ATF5	activating transcription factor 5	3
56052	ALG1	ALG1, chitobiosyldiphosphodolichol beta-mannosyltransferase	3
51099	ABHD5	abhydrolase domain containing 5	3
142940	TRUB1	TruB pseudouridine synthase family member 1	3
23729	SHPK	sedoheptulokinase	3
9016	SLC25A14	solute carrier family 25 member 14	3
10352	WARS2	tryptophanyl tRNA synthetase 2, mitochondrial	3
24140	FTSJ1	FtsJ RNA methyltransferase homolog 1 (E. coli)	3
23463	ICMT	isoprenylcysteine carboxyl methyltransferase	3
54974	THG1L	tRNA-histidine guanylyltransferase 1 like	3
124808	CCDC43	coiled-coil domain containing 43	3
5306	PITPNA	phosphatidylinositol transfer protein alpha	3
643155	SMIM15	small integral membrane protein 15	3
51260	PBDC1	polysaccharide biosynthesis domain containing 1	3
10200	MPHOSPH6	M-phase phosphoprotein 6	3
283578	TMED8	transmembrane p24 trafficking protein family member 8	3
79154	DHRS11	dehydrogenase/reductase 11	3
1743	DLST	dihydrolipoamide S-succinyltransferase	3
5277	PIGA	phosphatidylinositol glycan anchor biosynthesis class A	3
995	CDC25C	cell division cycle 25C	3
3833	KIFC1	kinesin family member C1	3
1967	EIF2B1	eukaryotic translation initiation factor 2B subunit alpha	3
119392	SFR1	SWI5 dependent homologous recombination repair protein 1	3
55795	PCID2	PCI domain containing 2	3
81542	TMX1	thioredoxin related transmembrane protein 1	3
55215	FANCI	Fanconi anemia complementation group I	3
23172	FAM175B	family with sequence similarity 175 member B	3
5711	PSMD5	proteasome 26S subunit, non-ATPase 5	3
153339	TMEM167A	transmembrane protein 167A	3

3842	TNPO1	transportin 1	3
84928	TMEM209	transmembrane protein 209	3
51263	MRPL30	mitochondrial ribosomal protein L30	3
7327	UBE2G2	ubiquitin conjugating enzyme E2 G2	3
23169	SLC35D1	solute carrier family 35 member D1	3
10617	STAMBP	STAM binding protein	3
8697	CDC23	cell division cycle 23	3
83930	STARD3NL	STARD3 N-terminal like	3
54556	ING3	inhibitor of growth family member 3	3
6185	RPN2	ribophorin II	3
253558	LCLAT1	lysocardiolipin acyltransferase 1	3
64710	NUCKS1	nuclear casein kinase and cyclin dependent kinase substrate 1	3
1635	DCTD	dCMP deaminase	3
91687	CENPL	centromere protein L	3
55308	DDX19A	DEAD-box helicase 19A	3
411	ARSB	arylsulfatase B	3
5889	RAD51C	RAD51 paralog C	3
7531	YWHAE	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein epsilon	3
79607	FAM118B	family with sequence similarity 118 member B	3
8883	NAE1	NEDD8 activating enzyme E1 subunit 1	3
2990	GUSB	glucuronidase beta	3
4076	CAPRIN1	cell cycle associated protein 1	3
4841	NONO	non-POU domain containing, octamer-binding	3
23511	NUP188	nucleoporin 188	3
54811	ZNF562	zinc finger protein 562	3
23279	NUP160	nucleoporin 160	3
10146	G3BP1	G3BP stress granule assembly factor 1	3
27085	MTBP	MDM2 binding protein	3
23310	NCAPD3	non-SMC condensin II complex subunit D3	3
6634	SNRPD3	small nuclear ribonucleoprotein D3 polypeptide	3
10920	COPS8	COP9 signalosome subunit 8	3
1678	TIMM8A	translocase of inner mitochondrial membrane 8 homolog A (yeast)	3
1798	DPAGT1	dolichyl-phosphate N-acetylglucosaminephosphotransferase 1	3
79135	APOO	apolipoprotein O	3
3187	HNRNPH1	heterogeneous nuclear ribonucleoprotein H1 (H)	3
89944	GLB1L2	galactosidase beta 1 like 2	3
5096	PCCB	propionyl-CoA carboxylase beta subunit	3
55254	TMEM39A	transmembrane protein 39A	3
6341	SCO1	SCO1, cytochrome c oxidase assembly protein	3
59067	IL21	interleukin 21	3
166968	MIER3	MIER family member 3	3
51524	TMEM138	transmembrane protein 138	3
7555	CNBP	CCHC-type zinc finger nucleic acid binding protein	3
57645	POGK	pogo transposable element with KRAB domain	3
1622	DBI	diazepam binding inhibitor, acyl-CoA binding protein	3
23741	EID1	EP300 interacting inhibitor of differentiation 1	3
84881	RPUSD4	RNA pseudouridylate synthase domain containing 4	3
79868	ALG13	ALG13, UDP-N-acetylglucosaminyltransferase subunit	3
10910	SUGT1	SGT1 homolog, MIS12 kinetochore complex assembly cochaperone	3
6902	TBCA	tubulin folding cofactor A	3
51094	ADIPOR1	adiponectin receptor 1	3
54534	MRPL50	mitochondrial ribosomal protein L50	3
5271	SERPINB8	serpin family B member 8	3
51318	MRPL35	mitochondrial ribosomal protein L35	3
9978	RBX1	ring-box 1	3
5885	RAD21	RAD21 cohesin complex component	3
9184	BUB3	BUB3, mitotic checkpoint protein	3
25847	ANAPC13	anaphase promoting complex subunit 13	3
25912	C1orf43	chromosome 1 open reading frame 43	3
9025	RNF8	ring finger protein 8	3
10959	TMED2	transmembrane p24 trafficking protein 2	3
1070	CETN3	centrin 3	3
7419	VDAC3	voltage dependent anion channel 3	3
5356	PLRG1	pleiotropic regulator 1	3
54529	ASNSD1	asparagine synthetase domain containing 1	3

51441	YTHDF2	YTH N6-methyladenosine RNA binding protein 2	3
5481	PPID	peptidylprolyl isomerase D	3
23098	SARM1	sterile alpha and TIR motif containing 1	3
22907	DHX30	DEAH-box helicase 30	3
65220	NADK	NAD kinase	3
201725	C4orf46	chromosome 4 open reading frame 46	3
2241	FER	FER tyrosine kinase	3
79598	CEP97	centrosomal protein 97	3
23760	PITPNB	phosphatidylinositol transfer protein beta	3
2965	GTF2H1	general transcription factor IIH subunit 1	3
6392	SDHD	succinate dehydrogenase complex subunit D	3
10001	MED6	mediator complex subunit 6	3
24145	PANX1	pannexin 1	3
26985	AP3M1	adaptor related protein complex 3 mu 1 subunit	3
54853	WDR55	WD repeat domain 55	3
9839	ZEB2	zinc finger E-box binding homeobox 2	3
5710	PSMD4	proteasome 26S subunit, non-ATPase 4	3
284695	ZNF326	zinc finger protein 326	3
598	BCL2L1	BCL2 like 1	3
29927	SEC61A1	Sec61 translocon alpha 1 subunit	3
91368	CDKN2AIPNL	CDKN2A interacting protein N-terminal like	3
51639	SF3B6	splicing factor 3b subunit 6	3
10483	SEC23B	Sec23 homolog B, coat complex II component	3
6732	SRPK1	SRSF protein kinase 1	3
9412	MED21	mediator complex subunit 21	3
80777	CYB5B	cytochrome b5 type B	3
5861	RAB1A	RAB1A, member RAS oncogene family	3
84191	FAM96A	family with sequence similarity 96 member A	3
4710	NDUFB4	NADH:ubiquinone oxidoreductase subunit B4	3
51538	ZCCHC17	zinc finger CCHC-type containing 17	3
7385	UQCRC2	ubiquinol-cytochrome c reductase core protein II	3
221443	OARD1	O-acyl-ADP-ribose deacylase 1	3
55101	ATP5SL	ATP5S like	3
51300	TIMMDC1	translocase of inner mitochondrial membrane domain containing 1	3
375	ARF1	ADP ribosylation factor 1	3
7979	SHFM1	split hand/foot malformation (ectrodactyly) type 1	3
5706	PSMC6	proteasome 26S subunit, ATPase 6	3
5092	PCBD1	pterin-4 alpha-carbinolamine dehydratase 1	3
58517	RBM25	RNA binding motif protein 25	3
10298	PAK4	p21 (RAC1) activated kinase 4	3
91942	NDUFAF2	NADH:ubiquinone oxidoreductase complex assembly factor 2	3
195827	AAED1	AhpC/TSA antioxidant enzyme domain containing 1	3
2960	GTF2E1	general transcription factor IIE subunit 1	3
509	ATP5C1	ATP synthase, H+ transporting, mitochondrial F1 complex, gamma polypeptide 1	3
84268	RPAIN	RPA interacting protein	3
8089	YEATS4	YEATS domain containing 4	3
9416	DDX23	DEAD-box helicase 23	3
466	ATF1	activating transcription factor 1	3
55151	TMEM38B	transmembrane protein 38B	3
84964	ALKBH6	alkB homolog 6	3
84950	PRPF38A	pre-mRNA processing factor 38A	3
64981	MRPL34	mitochondrial ribosomal protein L34	3
1827	RCAN1	regulator of calcineurin 1	3
51569	UFM1	ubiquitin fold modifier 1	3
57117	INTS12	integrator complex subunit 12	3
9588	PRDX6	peroxiredoxin 6	3
28978	TMEM14A	transmembrane protein 14A	3
7332	UBE2L3	ubiquitin conjugating enzyme E2 L3	3
378	ARF4	ADP ribosylation factor 4	3
51495	HACD3	3-hydroxyacyl-CoA dehydratase 3	3
9555	H2AFY	H2A histone family member Y	3
10635	RAD51AP1	RAD51 associated protein 1	3
11198	SUPT16H	SPT16 homolog, facilitates chromatin remodeling subunit	3
23595	ORC3	origin recognition complex subunit 3	3
30009	TBX21	T-box 21	3

5167	ENPP1	ectonucleotide pyrophosphatase/phosphodiesterase 1	3
28987	NOB1	NIN1/PSMD8 binding protein 1 homolog	3
7329	UBE2I	ubiquitin conjugating enzyme E2 I	3
246184	CDC26	cell division cycle 26	3
4712	NDUFB6	NADH:ubiquinone oxidoreductase subunit B6	3
253782	CERS6	ceramide synthase 6	3
11014	KDELR2	KDEL endoplasmic reticulum protein retention receptor 2	3
56943	ENY2	ENY2, transcription and export complex 2 subunit	3
440145	MZT1	mitotic spindle organizing protein 1	3
84128	WDR75	WD repeat domain 75	3
55660	PRPF40A	pre-mRNA processing factor 40 homolog A	3
23322	RPGRIP1L	RPGRIP1 like	3
3178	HNRNPA1	heterogeneous nuclear ribonucleoprotein A1	3
9275	BCL7B	BCL tumor suppressor 7B	3
65991	FUNDC2	FUN14 domain containing 2	3
64794	DDX31	DEAD-box helicase 31	3
8798	DYRK4	dual specificity tyrosine phosphorylation regulated kinase 4	3
55315	SLC29A3	solute carrier family 29 member 3	3
219541	MED19	mediator complex subunit 19	3
729993	SHISA9	shisa family member 9	3
8394	PIP5K1A	phosphatidylinositol-4-phosphate 5-kinase type 1 alpha	3
93487	MAPK1IP1L	mitogen-activated protein kinase 1 interacting protein 1 like	3
25994	HIGD1A	HIG1 hypoxia inducible domain family member 1A	3
87178	PNPT1	polyribonucleotide nucleotidyltransferase 1	3
6629	SNRPB2	small nuclear ribonucleoprotein polypeptide B2	3
25879	DCAF13	DDB1 and CUL4 associated factor 13	3
134430	WDR36	WD repeat domain 36	3
23658	LSM5	LSM5 homolog, U6 small nuclear RNA and mRNA degradation associated	3
9128	PRPF4	pre-mRNA processing factor 4	3
8891	EIF2B3	eukaryotic translation initiation factor 2B subunit gamma	3
10269	ZMPSTE24	zinc metallopeptidase STE24	3
498	ATP5A1	ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit 1, cardiac muscle	3
1738	DLD	dihydrolipoamide dehydrogenase	3
54332	GDAP1	ganglioside induced differentiation associated protein 1	3
85465	SELENOI	selenoprotein I	3
5701	PSMC2	proteasome 26S subunit, ATPase 2	3
3035	HARS	histidyl-tRNA synthetase	3
55361	PI4K2A	phosphatidylinositol 4-kinase type 2 alpha	3
5687	PSMA6	proteasome subunit alpha 6	3
23016	EXOSC7	exosome component 7	3
214	ALCAM	activated leukocyte cell adhesion molecule	3
2108	ETFA	electron transfer flavoprotein alpha subunit	3
29960	MRM2	mitochondrial rRNA methyltransferase 2	3
5690	PSMB2	proteasome subunit beta 2	3
3735	KARS	lysyl-tRNA synthetase	3
10666	CD226	CD226 molecule	3
10237	SLC35B1	solute carrier family 35 member B1	3
80218	NAA50	N(alpha)-acetyltransferase 50, NatE catalytic subunit	3
57476	GRAMD1B	GRAM domain containing 1B	3
10376	TUBA1B	tubulin alpha 1b	3
11102	RPP14	ribonuclease P/MRP subunit p14	3
11340	EXOSC8	exosome component 8	3
6717	SRI	sorcin	3
2395	FXN	frataxin	3
8872	CDC123	cell division cycle 123	3
8533	COPS3	COP9 signalosome subunit 3	3
79869	CPSF7	cleavage and polyadenylation specific factor 7	3
493856	CISD2	CDGSH iron sulfur domain 2	3
9319	TRIP13	thyroid hormone receptor interactor 13	3
54927	CHCHD3	coiled-coil-helix-coiled-coil-helix domain containing 3	3
10042	HMGXB4	HMG-box containing 4	3
55787	TXLNG	taxilin gamma	3
4522	MTHFD1	methylenetetrahydrofolate dehydrogenase, cyclohydrolase and formyltetrahydrofolate synthetase 1	3

10007	GNPDA1	glucosamine-6-phosphate deaminase 1	3
10229	COQ7	coenzyme Q7, hydroxylase	3
2079	ERH	enhancer of rudimentary homolog (Drosophila)	3
29796	UQCR10	ubiquinol-cytochrome c reductase, complex III subunit X	3
5705	PSMC5	proteasome 26S subunit, ATPase 5	3
128061	C1orf131	chromosome 1 open reading frame 131	3
10284	SAP18	Sin3A associated protein 18	3
3015	H2AFZ	H2A histone family member Z	3
54957	TXNL4B	thioredoxin like 4B	3
10944	C11orf58	chromosome 11 open reading frame 58	3
23788	MTCH2	mitochondrial carrier 2	3
6118	RPA2	replication protein A2	3
65260	COA7	cytochrome c oxidase assembly factor 7 (putative)	3
3419	IDH3A	isocitrate dehydrogenase 3 (NAD(+)) alpha	3
285381	DPH3	diphthamide biosynthesis 3	3
11103	KRR1	KRR1, small subunit processome component homolog	3
56942	CMC2	C-X9-C motif containing 2	3
5440	POLR2K	RNA polymerase II subunit K	3
326625	MMAB	methylmalonic aciduria (cobalamin deficiency) cblB type	3
23587	ELP5	elongator acetyltransferase complex subunit 5	3
57129	MRPL47	mitochondrial ribosomal protein L47	3
51202	DDX47	DEAD-box helicase 47	3
80273	GRPEL1	GrpE like 1, mitochondrial	3
79017	GGCT	gamma-glutamylcyclotransferase	3
401505	TOMM5	translocase of outer mitochondrial membrane 5	3
7353	UFD1L	ubiquitin fusion degradation 1 like (yeast)	3
54205	CYCS	cytochrome c, somatic	3
10289	EIF1B	eukaryotic translation initiation factor 1B	3
124637	CYB5D1	cytochrome b5 domain containing 1	3
27429	HTRA2	HtrA serine peptidase 2	3
5691	PSMB3	proteasome subunit beta 3	3
8683	SRSF9	serine and arginine rich splicing factor 9	3
78996	C7orf49	chromosome 7 open reading frame 49	3
81892	SLIRP	SRA stem-loop interacting RNA binding protein	3
30968	STOML2	stomatin like 2	3
55052	MRPL20	mitochondrial ribosomal protein L20	3
441531	PGAM4	phosphoglycerate mutase family member 4	3
7019	TFAM	transcription factor A, mitochondrial	3
55239	OGFOD1	2-oxoglutarate and iron dependent oxygenase domain containing 1	3
5515	PPP2CA	protein phosphatase 2 catalytic subunit alpha	3
4361	MRE11A	MRE11 homolog A, double strand break repair nuclease	3
5718	PSMD12	proteasome 26S subunit, non-ATPase 12	3
4528	MTIF2	mitochondrial translational initiation factor 2	3
10576	CCT2	chaperonin containing TCP1 subunit 2	3
529	ATP6V1E1	ATPase H+ transporting V1 subunit E1	3
150274	HSCB	HscB mitochondrial iron-sulfur cluster cochaperone	3
140609	NEK7	NIMA related kinase 7	3
113444	SMIM12	small integral membrane protein 12	3
10197	PSME3	proteasome activator subunit 3	3
152519	NIPAL1	NIPA like domain containing 1	3
506	ATP5B	ATP synthase, H+ transporting, mitochondrial F1 complex, beta polypeptide	3
5692	PSMB4	proteasome subunit beta 4	3
92400	RBM18	RNA binding motif protein 18	3
5110	PCMT1	protein-L-isoaspartate (D-aspartate) O-methyltransferase	3
10480	EIF3M	eukaryotic translation initiation factor 3 subunit M	3
4520	MTF1	metal regulatory transcription factor 1	3
526	ATP6V1B2	ATPase H+ transporting V1 subunit B2	3
7319	UBE2A	ubiquitin conjugating enzyme E2 A	3
4836	NMT1	N-myristoyltransferase 1	3
54470	ARMCX6	armadillo repeat containing, X-linked 6	3
56852	RAD18	RAD18, E3 ubiquitin protein ligase	3
10436	EMG1	EMG1, N1-specific pseudouridine methyltransferase	3
4704	NDUFA9	NADH:ubiquinone oxidoreductase subunit A9	3
27257	LSM1	LSM1 homolog, mRNA degradation associated	3
79719	AAGAB	alpha- and gamma-adaptin binding protein	3
25904	CNOT10	CCR4-NOT transcription complex subunit 10	3

8892	EIF2B2	eukaryotic translation initiation factor 2B subunit beta	3
892	CCNC	cyclin C	3
169200	TMEM64	transmembrane protein 64	3
56984	PSMG2	proteasome assembly chaperone 2	3
223	ALDH9A1	aldehyde dehydrogenase 9 family member A1	3
9330	GTF3C3	general transcription factor IIIC subunit 3	3
6184	RPN1	ribophorin I	3
116228	COX20	COX20, cytochrome c oxidase assembly factor	3
9967	THRAP3	thyroid hormone receptor associated protein 3	3
4725	NDUFS5	NADH:ubiquinone oxidoreductase subunit S5	3
80135	RPF1	ribosome production factor 1 homolog	3
5501	PPP1CC	protein phosphatase 1 catalytic subunit gamma	3
28511	NKIRAS2	NFKB inhibitor interacting Ras like 2	3
51234	EMC4	ER membrane protein complex subunit 4	3
10671	DCTN6	dynactin subunit 6	3
2631	GBAS	glioblastoma amplified sequence	3
23306	NEMP1	nuclear envelope integral membrane protein 1	3
10799	RPP40	ribonuclease P/MRP subunit p40	3
57563	KLHL8	kelch like family member 8	3
328	APEX1	apurinic/apyrimidinic endodeoxyribonuclease 1	3
90701	SEC11C	SEC11 homolog C, signal peptidase complex subunit	3
23480	SEC61G	Sec61 translocon gamma subunit	3
8819	SAP30	Sin3A associated protein 30	3
52	ACP1	acid phosphatase 1, soluble	3
1349	COX7B	cytochrome c oxidase subunit 7B	3
7386	UQCRFS1	ubiquinol-cytochrome c reductase, Rieske iron-sulfur polypeptide 1	3
26355	FAM162A	family with sequence similarity 162 member A	3
29074	MRPL18	mitochondrial ribosomal protein L18	3
79036	KXD1	KxDL motif containing 1	3
26156	RSL1D1	ribosomal L1 domain containing 1	3
55505	NOP10	NOP10 ribonucleoprotein	3
522	ATP5J	ATP synthase, H+ transporting, mitochondrial Fo complex subunit F6	3
387521	TMEM189	transmembrane protein 189	3
5547	PRCP	prolylcarboxypeptidase	3
26995	TRUB2	TruB pseudouridine synthase family member 2	3
153527	ZMAT2	zinc finger matrin-type 2	3
84126	ATRIP	ATR interacting protein	3
201931	TMEM192	transmembrane protein 192	3
4719	NDUFS1	NADH:ubiquinone oxidoreductase core subunit S1	3
27095	TRAPPC3	trafficking protein particle complex 3	3
9217	VAPB	VAMP associated protein B and C	3
10548	TM9SF1	transmembrane 9 superfamily member 1	3
55110	MAGOHB	mago homolog B, exon junction complex core component	3
9512	PMPCB	peptidase, mitochondrial processing beta subunit	3
58505	OSTC	oligosaccharyltransferase complex non-catalytic subunit	3
55071	C9orf40	chromosome 9 open reading frame 40	3
29086	BABAM1	BRISC and BRCA1 A complex member 1	3
327	APEH	acylaminoacyl-peptide hydrolase	3
221120	ALKBH3	alkB homolog 3, alpha-ketoglutaratedependent dioxygenase	3
79109	MAPKAP1	mitogen-activated protein kinase associated protein 1	3
375444	C5orf34	chromosome 5 open reading frame 34	3
113829	SLC35A4	solute carrier family 35 member A4	3
8350	HIST1H3A	histone cluster 1 H3 family member a	3
79760	GEMIN7	gem nuclear organelle associated protein 7	3
79002	C19orf43	chromosome 19 open reading frame 43	3
8407	TAGLN2	transgelin 2	3
5805	PTS	6-pyruvoyltetrahydropterin synthase	3
8226	PUDP	pseudouridine 5'-phosphatase	3
8330	HIST1H2AK	histone cluster 1 H2A family member k	3
6944	VPS72	vacuolar protein sorting 72 homolog	3
22913	RALY	RALY heterogeneous nuclear ribonucleoprotein	3
9793	CKAP5	cytoskeleton associated protein 5	3
11065	UBE2C	ubiquitin conjugating enzyme E2 C	3
81605	URM1	ubiquitin related modifier 1	3
6388	SDF2	stromal cell derived factor 2	3

8970	HIST1H2BJ	histone cluster 1 H2B family member j	3
8345	HIST1H2BH	histone cluster 1 H2B family member h	3
2491	CENPI	centromere protein I	3
5090	PBX3	PBX homeobox 3	3
24137	KIF4A	kinesin family member 4A	3
50943	FOXP3	forkhead box P3	3
8346	HIST1H2BI	histone cluster 1 H2B family member i	3
8357	HIST1H3H	histone cluster 1 H3 family member h	3
8368	HIST1H4L	histone cluster 1 H4 family member l	3
8355	HIST1H3G	histone cluster 1 H3 family member g	3
8348	HIST1H2BO	histone cluster 1 H2B family member o	3
734	OSGIN2	oxidative stress induced growth inhibitor family member 2	3
968	CD68	CD68 molecule	3
11004	KIF2C	kinesin family member 2C	3
80222	TARS2	threonyl-tRNA synthetase 2, mitochondrial (putative)	3
81603	TRIM8	tripartite motif containing 8	3
123606	NIPA1	non imprinted in Prader-Willi/Angelman syndrome 1	3
6046	BRD2	bromodomain containing 2	3
3006	HIST1H1C	histone cluster 1 H1 family member c	3
29916	SNX11	sorting nexin 11	3
9817	KEAP1	kelch like ECH associated protein 1	3
3996	LLGL1	LLGL1, scribble cell polarity complex component	3
5827	PXMP2	peroxisomal membrane protein 2	3
318	NUDT2	nudix hydrolase 2	3
117177	RAB3IP	RAB3A interacting protein	3
80227	PAAF1	proteasomal ATPase associated factor 1	3
116064	LRRC58	leucine rich repeat containing 58	3
56890	MDM1	Mdm1 nuclear protein	3
84058	WDR54	WD repeat domain 54	3
4087	SMAD2	SMAD family member 2	3
899	CCNF	cyclin F	3
8349	HIST2H2BE	histone cluster 2 H2B family member e	3
84193	SETD3	SET domain containing 3	3
140901	STK35	serine/threonine kinase 35	3
55704	CCDC88A	coiled-coil domain containing 88A	3
23132	RAD54L2	RAD54-like 2 (S. cerevisiae)	3
56672	AKIP1	A-kinase interacting protein 1	3
11218	DDX20	DEAD-box helicase 20	3
27291	R3HCC1L	R3H domain and coiled-coil containing 1 like	3
874	CBR3	carbonyl reductase 3	3
84959	UBASH3B	ubiquitin associated and SH3 domain containing B	3
10134	BCAP31	B-cell receptor-associated protein 31	3
4968	OGG1	8-oxoguanine DNA glycosylase	3
415116	PIM3	Pim-3 proto-oncogene, serine/threonine kinase	3
80199	FUZ	fuzzy planar cell polarity protein	3
967	CD63	CD63 molecule	3
84232	MAF1	MAF1 homolog, negative regulator of RNA polymerase III	3
572	BAD	BCL2 associated agonist of cell death	3
26608	TBL2	transducin beta like 2	3
5538	PPT1	palmitoyl-protein thioesterase 1	3
3008	HIST1H1E	histone cluster 1 H1 family member e	3
65062	TMEM237	transmembrane protein 237	3
8294	HIST1H4I	histone cluster 1 H4 family member i	3
8335	HIST1H2AB	histone cluster 1 H2A family member b	3
3024	HIST1H1A	histone cluster 1 H1 family member a	3
439	ASNA1	arsA arsenite transporter, ATP-binding, homolog 1 (bacterial)	3
2805	GOT1	glutamic-oxaloacetic transaminase 1	3
57539	WDR35	WD repeat domain 35	3
163786	SASS6	SAS-6 centriolar assembly protein	3
3189	HNRNPH3	heterogeneous nuclear ribonucleoprotein H3	3
85236	HIST1H2BK	histone cluster 1 H2B family member k	3
5881	RAC3	ras-related C3 botulinum toxin substrate 3 (rho family, small GTP binding protein Rac3)	3
10614	HEXIM1	hexamethylene bisacetamide inducible 1	3
283464	GXYLT1	glucoside xylosyltransferase 1	3

3014	H2AFX	H2A histone family member X	3
25853	DCAF12	DDB1 and CUL4 associated factor 12	3
56994	CHPT1	choline phosphotransferase 1	3
9551	ATP5J2	ATP synthase, H+ transporting, mitochondrial Fo complex subunit F2	3
27304	MOCS3	molybdenum cofactor synthesis 3	3
113130	CDCA5	cell division cycle associated 5	3
81887	LAS1L	LAS1 like, ribosome biogenesis factor	3
5201	PFDN1	prefoldin subunit 1	3
91057	CCDC34	coiled-coil domain containing 34	3
468	ATF4	activating transcription factor 4	3
161823	ADAL	adenosine deaminase like	3
55723	ASF1B	anti-silencing function 1B histone chaperone	3
91442	FAAP24	Fanconi anemia core complex associated protein 24	3
220002	CYB561A3	cytochrome b561 family member A3	3
84759	PCGF1	polycomb group ring finger 1	3
112950	MED8	mediator complex subunit 8	3
587	BCAT2	branched chain amino acid transaminase 2	3
643	CXCR5	C-X-C motif chemokine receptor 5	3
55794	DDX28	DEAD-box helicase 28	3
6470	SHMT1	serine hydroxymethyltransferase 1	3
10651	MTX2	metaxin 2	3
54921	CHTF8	chromosome transmission fidelity factor 8	3
51283	BFAR	bifunctional apoptosis regulator	3
57456	KIAA1143	KIAA1143	3
54995	OXSM	3-oxoacyl-ACP synthase, mitochondrial	3
79102	RNF26	ring finger protein 26	3
79000	AUNIP	aurora kinase A and ninein interacting protein	3
4947	OAZ2	ornithine decarboxylase antizyme 2	3
25979	DHRS7B	dehydrogenase/reductase 7B	3
23052	ENDOD1	endonuclease domain containing 1	3
728568	C12orf73	chromosome 12 open reading frame 73	3
54890	ALKBH5	alkB homolog 5, RNA demethylase	3
348793	WDR53	WD repeat domain 53	3
57045	TWSG1	twisted gastrulation BMP signaling modulator 1	3
84844	PHF5A	PHD finger protein 5A	3
79228	THOC6	THO complex 6	3
27235	COQ2	coenzyme Q2, polyprenyltransferase	3
170371	C10orf128	chromosome 10 open reading frame 128	3
1861	TOR1A	torsin family 1 member A	3
150771	ITPRIPL1	inositol 1,4,5-trisphosphate receptor interacting protein-like 1	3
56180	MOSPD1	motile sperm domain containing 1	3
4702	NDUFA8	NADH:ubiquinone oxidoreductase subunit A8	3
55246	CCDC25	coiled-coil domain containing 25	3
5684	PSMA3	proteasome subunit alpha 3	3
54942	FAM206A	family with sequence similarity 206 member A	3
9836	LCMT2	leucine carboxyl methyltransferase 2	3
55344	PLCXD1	phosphatidylinositol specific phospholipase C X domain containing 1	3
49854	ZBTB21	zinc finger and BTB domain containing 21	3
25926	NOL11	nucleolar protein 11	3
1854	DUT	deoxyuridine triphosphatase	3
662	BNIP1	BCL2 interacting protein 1	3
29928	TIMM22	translocase of inner mitochondrial membrane 22 homolog	3
78988	MRPL57	mitochondrial ribosomal protein L57	3
121642	ALKBH2	alkB homolog 2, alpha-ketoglutarate dependent dioxygenase	3
10535	RNASEH2A	ribonuclease H2 subunit A	3
339230	CCDC137	coiled-coil domain containing 137	3
51399	TRAPPC4	trafficking protein particle complex 4	3
23239	PHLPP1	PH domain and leucine rich repeat protein phosphatase 1	3
23212	RRS1	ribosome biogenesis regulator homolog	3
26520	TIMM9	translocase of inner mitochondrial membrane 9	3
84879	MFSD2A	major facilitator superfamily domain containing 2A	3
28973	MRPS18B	mitochondrial ribosomal protein S18B	3
118472	ZNF511	zinc finger protein 511	3
8531	YBX3	Y-box binding protein 3	3
746	TMEM258	transmembrane protein 258	3

147007	TMEM199	transmembrane protein 199	3
55829	SELENOS	selenoprotein S	3
23478	SEC11A	SEC11 homolog A, signal peptidase complex subunit	3
5713	PSMD7	proteasome 26S subunit, non-ATPase 7	3
65005	MRPL9	mitochondrial ribosomal protein L9	3
27301	APEX2	apurinic/apyrimidinic endodeoxyribonuclease 2	3
27315	PGAP2	post-GPI attachment to proteins 2	3
27075	TSPAN13	tetraspanin 13	3
6396	SEC13	SEC13 homolog, nuclear pore and COPII coat complex component	3
29101	SSU72	SSU72 homolog, RNA polymerase II CTD phosphatase	3
79035	NABP2	nucleic acid binding protein 2	3
5160	PDHA1	pyruvate dehydrogenase (lipoamide) alpha 1	3
115416	MALSU1	mitochondrial assembly of ribosomal large subunit 1	3
9218	VAPA	VAMP associated protein A	3
3396	MRPL58	mitochondrial ribosomal protein L58	3
64976	MRPL40	mitochondrial ribosomal protein L40	3
1123	CHN1	chimerin 1	3
149603	RNF187	ring finger protein 187	3
84246	MED10	mediator complex subunit 10	3
7260	TSSC1	tumor suppressing subtransferable candidate 1	3
10084	PQBP1	polyglutamine binding protein 1	3
661	POLR3D	RNA polymerase III subunit D	3
56257	MEPCE	methylphosphate capping enzyme	3
9371	KIF3B	kinesin family member 3B	3
92002	FAM58A	family with sequence similarity 58 member A	3
114049	WBSCR22	Williams-Beuren syndrome chromosome region 22	3
55038	CDCA4	cell division cycle associated 4	3
339263	C17orf51	chromosome 17 open reading frame 51	3
11137	PWP1	PWP1 homolog, endonuclein	3
55278	QRSL1	glutaminyl-tRNA synthase (glutamine-hydrolyzing)-like 1	3
8811	GALR2	galanin receptor 2	3
118424	UBE2J2	ubiquitin conjugating enzyme E2 J2	3
3596	IL13	interleukin 13	3
7918	GPANK1	G-patch domain and ankyrin repeats 1	3
376267	RAB15	RAB15, member RAS oncogene family	3
8754	ADAM9	ADAM metallopeptidase domain 9	3
22916	NCBP2	nuclear cap binding protein subunit 2	3
79172	CENPO	centromere protein O	3
84547	PGBD1	piggyBac transposable element derived 1	3
28960	DCPS	decapping enzyme, scavenger	3
10741	RBBP9	RB binding protein 9, serine hydrolase	3
283106	CSNK2A3	casein kinase 2 alpha 3	3
84065	TMEM222	transmembrane protein 222	3
5686	PSMA5	proteasome subunit alpha 5	3
6573	SLC19A1	solute carrier family 19 member 1	3
51634	RBMX2	RNA binding motif protein, X-linked 2	3
54802	TRIT1	tRNA isopentenyltransferase 1	3
10280	SIGMAR1	sigma non-opioid intracellular receptor 1	3
5496	PPM1G	protein phosphatase, Mg2+/Mn2+ dependent 1G	3
970	CD70	CD70 molecule	3
9289	ADGRG1	adhesion G protein-coupled receptor G1	3
115939	TSR3	TSR3, acp transferase ribosome maturation factor	3
550	AUP1	ancient ubiquitous protein 1	3
9560	CCL4L2	C-C motif chemokine ligand 4 like 2	3
3567	IL5	interleukin 5	3
91319	DERL3	derlin 3	3
5743	PTGS2	prostaglandin-endoperoxide synthase 2	3
3703	STT3A	STT3A, catalytic subunit of the oligosaccharyltransferase complex	3
118980	SFXN2	sideroflexin 2	3
3578	IL9	interleukin 9	3
10276	NET1	neuroepithelial cell transforming 1	3
6348	CCL3	C-C motif chemokine ligand 3	3
10201	NME6	NME/NM23 nucleoside diphosphate kinase 6	3
84296	GINS4	GINS complex subunit 4	3
200933	FBXO45	F-box protein 45	3

9050	PSTPIP2	proline-serine-threonine phosphatase interacting protein 2	3
8356	HIST1H3J	histone cluster 1 H3 family member j	3
64745	METTL17	methyltransferase like 17	3
53838	C11orf24	chromosome 11 open reading frame 24	3
10293	TRAIP	TRAF interacting protein	3
51023	MRPS18C	mitochondrial ribosomal protein S18C	3
26150	RIBC2	RIB43A domain with coiled-coils 2	3
4049	LTA	lymphotoxin alpha	3
25828	TXN2	thioredoxin 2	3
5886	RAD23A	RAD23 homolog A, nucleotide excision repair protein	3
84522	JAGN1	jagunal homolog 1	3
128178	EDARADD	EDAR associated death domain	3
51163	DBR1	debranching RNA lariats 1	3
84545	MRPL43	mitochondrial ribosomal protein L43	3
84311	MRPL45	mitochondrial ribosomal protein L45	3
132720	C4orf32	chromosome 4 open reading frame 32	3
3775	KCNK1	potassium two pore domain channel subfamily K member 1	3
54069	MIS18A	MIS18 kinetochore protein A	3
55255	WDR41	WD repeat domain 41	3
9334	B4GALT5	beta-1,4-galactosyltransferase 5	3
80262	C16orf70	chromosome 16 open reading frame 70	3
55122	AKIRIN2	akirin 2	3
81610	FAM83D	family with sequence similarity 83 member D	3
55116	TMEM39B	transmembrane protein 39B	3
7976	FZD3	frizzled class receptor 3	3
83693	HSDL1	hydroxysteroid dehydrogenase like 1	3
5571	PRKAG1	protein kinase AMP-activated non-catalytic subunit gamma 1	3
6839	SUV39H1	suppressor of variegation 3-9 homolog 1	3
3052	HCCS	holocytochrome c synthase	3
1435	CSF1	colony stimulating factor 1	3
4682	NUBP1	nucleotide binding protein 1	3
873	CBR1	carbonyl reductase 1	3
4605	MYBL2	MYB proto-oncogene like 2	3
84057	MND1	meiotic nuclear divisions 1	3
2617	GARS	glycyl-tRNA synthetase	3
55148	UBR7	ubiquitin protein ligase E3 component n-recognin 7 (putative)	3
6241	RRM2	ribonucleotide reductase regulatory subunit M2	3
91801	ALKBH8	alkB homolog 8, tRNA methyltransferase	3
195828	ZNF367	zinc finger protein 367	3
54541	DDIT4	DNA damage inducible transcript 4	3
4292	MLH1	mutL homolog 1	3
9837	GINS1	GINS complex subunit 1	3
27000	DNAJC2	DnaJ heat shock protein family (Hsp40) member C2	3
55005	RMND1	required for meiotic nuclear division 1 homolog	3
5715	PSMD9	proteasome 26S subunit, non-ATPase 9	3
220134	SKA1	spindle and kinetochore associated complex subunit 1	3
55322	C5orf22	chromosome 5 open reading frame 22	3
890	CCNA2	cyclin A2	3
9833	MELK	maternal embryonic leucine zipper kinase	3
64151	NCAPG	non-SMC condensin I complex subunit G	3
4860	PNP	purine nucleoside phosphorylase	3
8846	ALKBH1	alkB homolog 1, histone H2A dioxygenase	3
23397	NCAPH	non-SMC condensin I complex subunit H	3
79733	E2F8	E2F transcription factor 8	3
55872	PBK	PDZ binding kinase	3
11079	RER1	retention in endoplasmic reticulum sorting receptor 1	3
51290	ERGIC2	ERGIC and golgi 2	3
6729	SRP54	signal recognition particle 54	3
121441	NEDD1	neural precursor cell expressed, developmentally down-regulated 1	3
983	CDK1	cyclin dependent kinase 1	3
6734	SRPRA	SRP receptor alpha subunit	3
10438	C1D	C1D nuclear receptor corepressor	3
11212	PROSC	proline synthetase cotranscribed homolog (bacterial)	3
79023	NUP37	nucleoporin 37	3
54433	GAR1	GAR1 ribonucleoprotein	3

6504	SLAMF1	signaling lymphocytic activation molecule family member 1	3
23107	MRPS27	mitochondrial ribosomal protein S27	3
9585	KIF20B	kinesin family member 20B	3
959	CD40LG	CD40 ligand	3
4218	RAB8A	RAB8A, member RAS oncogene family	3
23549	DNPEP	aspartyl aminopeptidase	3
7272	TTK	TTK protein kinase	3
84920	ALG10	ALG10, alpha-1,2-glucosyltransferase	3
2218	FKTN	fukutin	3
1786	DNMT1	DNA methyltransferase 1	3
29078	NDUFAF4	NADH:ubiquinone oxidoreductase complex assembly factor 4	3
144455	E2F7	E2F transcription factor 7	3
25983	NGDN	neuroguidin	3
11051	NUDT21	nudix hydrolase 21	3
6426	SRSF1	serine and arginine rich splicing factor 1	3
348995	NUP43	nucleoporin 43	3
81556	VWA9	von Willebrand factor A domain containing 9	3
286826	LIN9	lin-9 DREAM MuvB core complex component	3
10615	SPAG5	sperm associated antigen 5	3
10721	POLQ	DNA polymerase theta	3
25800	SLC39A6	solute carrier family 39 member 6	3
26958	COPG2	coatomer protein complex subunit gamma 2	3
5894	RAF1	Raf-1 proto-oncogene, serine/threonine kinase	3
8669	EIF3J	eukaryotic translation initiation factor 3 subunit J	3
9131	AIFM1	apoptosis inducing factor, mitochondria associated 1	3
28969	BZW2	basic leucine zipper and W2 domains 2	3
9136	RRP9	ribosomal RNA processing 9, small subunit (SSU) processome component, homolog (yeast)	3
11033	ADAP1	ArfGAP with dual PH domains 1	3
9377	COX5A	cytochrome c oxidase subunit 5A	3
51103	NDUFAF1	NADH:ubiquinone oxidoreductase complex assembly factor 1	3
196264	MPZL3	myelin protein zero like 3	3
83732	RIOK1	RIO kinase 1	3
116092	DNTTIP1	deoxynucleotidyltransferase terminal interacting protein 1	3
8480	RAE1	ribonucleic acid export 1	3
9556	C14orf2	chromosome 14 open reading frame 2	3
403	ARL3	ADP ribosylation factor like GTPase 3	3
10542	LAMTOR5	late endosomal/lysosomal adaptor, MAPK and MTOR activator 5	3
23365	ARHGEF12	Rho guanine nucleotide exchange factor 12	3
56947	MFF	mitochondrial fission factor	3
84233	TMEM126A	transmembrane protein 126A	3
3422	IDI1	isopentenyl-diphosphate delta isomerase 1	3
81502	HM13	histocompatibility minor 13	3
27339	PRPF19	pre-mRNA processing factor 19	3
9875	URB1	URB1 ribosome biogenesis 1 homolog (S. cerevisiae)	3
8454	CUL1	cullin 1	3
51232	CRIM1	cysteine rich transmembrane BMP regulator 1	3
9675	TTI1	TELO2 interacting protein 1	3
9373	PLAA	phospholipase A2 activating protein	3
4849	CNOT3	CCR4-NOT transcription complex subunit 3	3
9261	MAPKAPK2	mitogen-activated protein kinase-activated protein kinase 2	3
2926	GRSF1	G-rich RNA sequence binding factor 1	3
54931	TRMT10C	tRNA methyltransferase 10C, mitochondrial RNase P subunit	3
140465	MYL6B	myosin light chain 6B	3
64374	SIL1	SIL1 nucleotide exchange factor	3
51388	NIP7	NIP7, nucleolar pre-rRNA processing protein	3
2037	EPB41L2	erythrocyte membrane protein band 4.1 like 2	3
2146	EZH2	enhancer of zeste 2 polycomb repressive complex 2 subunit	3
1503	CTPS1	CTP synthase 1	3
51056	LAP3	leucine aminopeptidase 3	3
64422	ATG3	autophagy related 3	3
64425	POLR1E	RNA polymerase I subunit E	3
5876	RABGGTB	Rab geranylgeranyltransferase beta subunit	3
27340	UTP20	UTP20, small subunit processome component	3
79954	NOL10	nucleolar protein 10	3

10885	WDR3	WD repeat domain 3	3
467	ATF3	activating transcription factor 3	3
10775	POP4	POP4 homolog, ribonuclease P/MRP subunit	3
27166	PRELID1	PRELI domain containing 1	3
56945	MRPS22	mitochondrial ribosomal protein S22	3
821	CANX	calnexin	3
10525	HYOU1	hypoxia up-regulated 1	3
7037	TFRC	transferrin receptor	3
56005	MYDGF	myeloid derived growth factor	3
9879	DDX46	DEAD-box helicase 46	3
55131	RBM28	RNA binding motif protein 28	3
55920	RCC2	regulator of chromosome condensation 2	3
3954	LETM1	leucine zipper and EF-hand containing transmembrane protein 1	3
23603	CORO1C	coronin 1C	3
54948	MRPL16	mitochondrial ribosomal protein L16	3
22894	DIS3	DIS3 homolog, exosome endoribonuclease and 3'-5' exoribonuclease	3
51249	TMEM69	transmembrane protein 69	3
7873	MANF	mesencephalic astrocyte derived neurotrophic factor	3
5393	EXOSC9	exosome component 9	3
23197	FAF2	Fas associated factor family member 2	3
5888	RAD51	RAD51 recombinase	3
23761	PISD	phosphatidylserine decarboxylase	3
125061	AFMID	arylformamidase	3
5019	OXCT1	3-oxoacid CoA-transferase 1	3
53371	NUP54	nucleoporin 54	3
23404	EXOSC2	exosome component 2	3
8208	CHAF1B	chromatin assembly factor 1 subunit B	3
6240	RRM1	ribonucleotide reductase catalytic subunit M1	3
78995	C17orf53	chromosome 17 open reading frame 53	3
84930	MASTL	microtubule associated serine/threonine kinase like	3
51514	DTL	denticleless E3 ubiquitin protein ligase homolog	3
3837	KPNB1	karyopherin subunit beta 1	3
9156	EXO1	exonuclease 1	3
51194	IPO11	importin 11	3
10036	CHAF1A	chromatin assembly factor 1 subunit A	3
160897	GPR180	G protein-coupled receptor 180	3
8243	SMC1A	structural maintenance of chromosomes 1A	3
1122	CHML	CHM like, Rab escort protein 2	3
22984	PDCD11	programmed cell death 11	3
488	ATP2A2	ATPase sarcoplasmic/endoplasmic reticulum Ca2+ transporting 2	3
1874	E2F4	E2F transcription factor 4	3
55746	NUP133	nucleoporin 133	3
55973	BCAP29	B-cell receptor associated protein 29	3
84271	POLDIP3	DNA polymerase delta interacting protein 3	3
55127	HEATR1	HEAT repeat containing 1	3
128869	PIGU	phosphatidylinositol glycan anchor biosynthesis class U	3
79053	ALG8	ALG8, alpha-1,3-glucosyltransferase	3
2956	MSH6	mutS homolog 6	3
57678	GPAM	glycerol-3-phosphate acyltransferase, mitochondrial	3
9401	RECQL4	RecQ like helicase 4	3
79796	ALG9	ALG9, alpha-1,2-mannosyltransferase	3
993	CDC25A	cell division cycle 25A	3
56926	NCLN	nicalin	3
9816	URB2	URB2 ribosome biogenesis 2 homolog (S. cerevisiae)	3
10560	SLC19A2	solute carrier family 19 member 2	3
80223	RAB11FIP1	RAB11 family interacting protein 1	3
9733	SART3	squamous cell carcinoma antigen recognized by T-cells 3	3
22934	RPIA	ribose 5-phosphate isomerase A	3
10531	PITRM1	pitrilysin metallopeptidase 1	3
3251	HPRT1	hypoxanthine phosphoribosyltransferase 1	3
8833	GMPS	guanine monophosphate synthase	3
2175	FANCA	Fanconi anemia complementation group A	3
25788	RAD54B	RAD54 homolog B (S. cerevisiae)	3
80155	NAA15	N(alpha)-acetyltransferase 15, NatA auxiliary subunit	3
79723	SUV39H2	suppressor of variegation 3-9 homolog 2	3
132789	GNPDA2	glucosamine-6-phosphate deaminase 2	3

23234	DNAJC9	DnaJ heat shock protein family (Hsp40) member C9	3
57510	XPO5	exportin 5	3
6119	RPA3	replication protein A3	3
39	ACAT2	acetyl-CoA acetyltransferase 2	3
7993	UBXN8	UBX domain protein 8	3
10105	PPIF	peptidylprolyl isomerase F	3
57003	CCDC47	coiled-coil domain containing 47	3
57415	C3orf14	chromosome 3 open reading frame 14	3
10652	YKT6	YKT6 v-SNARE homolog (S. cerevisiae)	3
7374	UNG	uracil DNA glycosylase	3
51602	NOP58	NOP58 ribonucleoprotein	3
6566	SLC16A1	solute carrier family 16 member 1	3
4173	MCM4	minichromosome maintenance complex component 4	3
894	CCND2	cyclin D2	3
9790	BMS1	BMS1, ribosome biogenesis factor	3
51118	UTP11	UTP11, small subunit processome component homolog (S. cerevisiae)	3
51126	NAA20	N(alpha)-acetyltransferase 20, NatB catalytic subunit	3
10950	BTG3	BTG anti-proliferation factor 3	3
10574	CCT7	chaperonin containing TCP1 subunit 7	3
55646	LYAR	Ly1 antibody reactive	3
84319	CMSS1	cms1 ribosomal small subunit homolog (yeast)	3
120425	JAML	junction adhesion molecule like	3
10471	PFDN6	prefoldin subunit 6	3
51497	NELFCD	negative elongation factor complex member C/D	3
131076	CCDC58	coiled-coil domain containing 58	3
2067	ERCC1	ERCC excision repair 1, endonuclease non-catalytic subunit	3
55299	BRIX1	BRX1, biogenesis of ribosomes	3
8520	HAT1	histone acetyltransferase 1	3
1845	DUSP3	dual specificity phosphatase 3	3
2321	FLT1	fms related tyrosine kinase 1	3
5422	POLA1	DNA polymerase alpha 1, catalytic subunit	3
55759	WDR12	WD repeat domain 12	3
26010	SPATS2L	spermatogenesis associated serine rich 2 like	3
5887	RAD23B	RAD23 homolog B, nucleotide excision repair protein	3
23516	SLC39A14	solute carrier family 39 member 14	3
83743	GRWD1	glutamate rich WD repeat containing 1	3
5702	PSMC3	proteasome 26S subunit, ATPase 3	3
54487	DGCR8	DGCR8, microprocessor complex subunit	3
55720	TSR1	TSR1, ribosome maturation factor	3
2547	XRCC6	X-ray repair cross complementing 6	3
5982	RFC2	replication factor C subunit 2	3
27346	TMEM97	transmembrane protein 97	3
80179	MYO19	myosin XIX	3
9343	EFTUD2	elongation factor Tu GTP binding domain containing 2	3
220042	DDIAS	DNA damage induced apoptosis suppressor	3
8318	CDC45	cell division cycle 45	3
5471	PPAT	phosphoribosyl pyrophosphate amidotransferase	3
990	CDC6	cell division cycle 6	3
90861	HN1L	hematological and neurological expressed 1 like	3
29128	UHRF1	ubiquitin like with PHD and ring finger domains 1	3
1111	CHEK1	checkpoint kinase 1	3
55854	ZC3H15	zinc finger CCCH-type containing 15	3
4998	ORC1	origin recognition complex subunit 1	3
5111	PCNA	proliferating cell nuclear antigen	3
54962	TIPIN	TIMELESS interacting protein	3
51377	UCHL5	ubiquitin C-terminal hydrolase L5	3
9125	CNOT9	CCR4-NOT transcription complex subunit 9	3
11222	MRPL3	mitochondrial ribosomal protein L3	3
1965	EIF2S1	eukaryotic translation initiation factor 2 subunit alpha	3
6427	SRSF2	serine and arginine rich splicing factor 2	3
10623	POLR3C	RNA polymerase III subunit C	3
7884	SLBP	stem-loop binding protein	3
79622	SNRNP25	small nuclear ribonucleoprotein U11/U12 subunit 25	3
4172	MCM3	minichromosome maintenance complex component 3	3
2237	FEN1	flap structure-specific endonuclease 1	3

171568	POLR3H	RNA polymerase III subunit H	3
8704	B4GALT2	beta-1,4-galactosyltransferase 2	3
55388	MCM10	minichromosome maintenance 10 replication initiation factor	3
26509	MYOF	myoferlin	3
94097	SFXN5	sideroflexin 5	3
55379	LRRC59	leucine rich repeat containing 59	3
2271	FH	fumarate hydratase	3
26284	ERAL1	Era like 12S mitochondrial rRNA chaperone 1	3
2958	GTF2A2	general transcription factor IIA subunit 2	3
1869	E2F1	E2F transcription factor 1	3
11332	ACOT7	acyl-CoA thioesterase 7	3
898	CCNE1	cyclin E1	3
5983	RFC3	replication factor C subunit 3	3
3021	H3F3B	H3 histone family member 3B	3
10419	PRMT5	protein arginine methyltransferase 5	3
64858	DCLRE1B	DNA cross-link repair 1B	3
10054	UBA2	ubiquitin like modifier activating enzyme 2	3
2176	FANCC	Fanconi anemia complementation group C	3
51124	IER3IP1	immediate early response 3 interacting protein 1	3
126526	C19orf47	chromosome 19 open reading frame 47	3
60386	SLC25A19	solute carrier family 25 member 19	3
56910	STARD7	StAR related lipid transfer domain containing 7	3
3976	LIF	leukemia inhibitory factor	3
1841	DTYMK	deoxythymidylate kinase	3
10556	RPP30	ribonuclease P/MRP subunit p30	3
10360	NPM3	nucleophosmin/nucleoplasmin 3	3
114034	TOE1	target of EGR1, member 1 (nuclear)	3
79693	YRDC	yrdC N6-threonylcarbamoyltransferase domain containing	3
5631	PRPS1	phosphoribosyl pyrophosphate synthetase 1	3
56851	EMC7	ER membrane protein complex subunit 7	3
10949	HNRNPA0	heterogeneous nuclear ribonucleoprotein A0	3
51559	NT5DC3	5'-nucleotidase domain containing 3	3
79682	CENPU	centromere protein U	3
9410	SNRNP40	small nuclear ribonucleoprotein U5 subunit 40	3
8624	PSMG1	proteasome assembly chaperone 1	3
5557	PRIM1	primase (DNA) subunit 1	3
55159	RFWD3	ring finger and WD repeat domain 3	3
29089	UBE2T	ubiquitin conjugating enzyme E2 T	3
84515	MCM8	minichromosome maintenance 8 homologous recombination repair factor	3
11164	NUDT5	nudix hydrolase 5	3
203068	TUBB	tubulin beta class I	3
6472	SHMT2	serine hydroxymethyltransferase 2	3
132	ADK	adenosine kinase	3
401541	CENPP	centromere protein P	3
805	CALM2	calmodulin 2	3
4616	GADD45B	growth arrest and DNA damage inducible beta	3
10328	EMC8	ER membrane protein complex subunit 8	3
5546	PRCC	papillary renal cell carcinoma (translocation-associated)	3
1164	CKS2	CDC28 protein kinase regulatory subunit 2	3
27242	TNFRSF21	TNF receptor superfamily member 21	3
9318	COPS2	COP9 signalosome subunit 2	3
56993	TOMM22	translocase of outer mitochondrial membrane 22	3
84549	MAK16	MAK16 homolog	3
5437	POLR2H	RNA polymerase II subunit H	3
388272	C16orf87	chromosome 16 open reading frame 87	3
113115	MTFR2	mitochondrial fission regulator 2	3
4043	LRPAP1	LDL receptor related protein associated protein 1	3
55347	ABHD10	abhydrolase domain containing 10	3
79968	WDR76	WD repeat domain 76	3
262	AMD1	adenosylmethionine decarboxylase 1	3
27131	SNX5	sorting nexin 5	3
93081	TEX30	testis expressed 30	3
200081	TXLNA	taxilin alpha	3
84334	APOPT1	apoptogenic 1, mitochondrial	3
8836	GGH	gamma-glutamyl hydrolase	3

1528	CYB5A	cytochrome b5 type A	3
122769	LRR1	leucine rich repeat protein 1	3
8896	BUD31	BUD31 homolog	3
7922	SLC39A7	solute carrier family 39 member 7	3
83903	GSG2	germ cell associated 2, haspin	3
79019	CENPM	centromere protein M	3
10038	PARP2	poly(ADP-ribose) polymerase 2	3
11130	ZWINT	ZW10 interacting kinetochore protein	3
91	ACVR1B	activin A receptor type 1B	3
6742	SSBP1	single stranded DNA binding protein 1	3
7398	USP1	ubiquitin specific peptidase 1	3
79980	DSN1	DSN1 homolog, MIS12 kinetochore complex component	3
9134	CCNE2	cyclin E2	3
387103	CENPW	centromere protein W	3
9984	THOC1	THO complex 1	3
23421	ITGB3BP	integrin subunit beta 3 binding protein	3
54108	CHRAC1	chromatin accessibility complex 1	3
79801	SHCBP1	SHC binding and spindle associated 1	3
3185	HNRNPF	heterogeneous nuclear ribonucleoprotein F	3
813	CALU	calumenin	3
10733	PLK4	polo like kinase 4	3
211	ALAS1	5'-aminolevulinate synthase 1	3
81831	NETO2	neuropilin and tolloid like 2	3
79001	VKORC1	vitamin K epoxide reductase complex subunit 1	3
26123	TCTN3	tectonic family member 3	3
25896	INTS7	integrator complex subunit 7	3
64834	ELOVL1	ELOVL fatty acid elongase 1	3
80304	WDCP	WD repeat and coiled coil containing	3
51550	CINP	cyclin dependent kinase 2 interacting protein	3
38	ACAT1	acetyl-CoA acetyltransferase 1	3
79084	WDR77	WD repeat domain 77	3
219988	PATL1	PAT1 homolog 1, processing body mRNA decay factor	3
63979	FIGNL1	fidgetin like 1	3
10772	SRSF10	serine and arginine rich splicing factor 10	3
6788	STK3	serine/threonine kinase 3	3
85459	CEP295	centrosomal protein 295	3
2746	GLUD1	glutamate dehydrogenase 1	3
58490	RPRD1B	regulation of nuclear pre-mRNA domain containing 1B	3
3005	H1F0	H1 histone family member 0	3
55163	PNPO	pyridoxamine 5'-phosphate oxidase	3
114134	SLC2A13	solute carrier family 2 member 13	3
7384	UQCRC1	ubiquinol-cytochrome c reductase core protein I	3
23509	POFUT1	protein O-fucosyltransferase 1	3
975	CD81	CD81 molecule	3
7408	VASP	vasodilator-stimulated phosphoprotein	3
93323	HAUS8	HAUS augmin like complex subunit 8	3
124535	HSF5	heat shock transcription factor 5	3
85444	LRRCC1	leucine rich repeat and coiled-coil centrosomal protein 1	3
51150	SDF4	stromal cell derived factor 4	3
56919	DHX33	DEAH-box helicase 33	3
23035	PHLPP2	PH domain and leucine rich repeat protein phosphatase 2	3
8879	SGPL1	sphingosine-1-phosphate lyase 1	3
51593	SRRT	serrate, RNA effector molecule	3
790	CAD	carbamoyl-phosphate synthetase 2, aspartate transcarbamylase, and dihydroorotase	3
6541	SLC7A1	solute carrier family 7 member 1	3
6835	SURF2	surfeit 2	3
84306	PDCD2L	programmed cell death 2 like	3
51693	TRAPPC2L	trafficking protein particle complex 2 like	3
7001	PRDX2	peroxiredoxin 2	3
22976	PAXIP1	PAX interacting protein 1	3
51692	CPSF3	cleavage and polyadenylation specific factor 3	3
11193	WBP4	WW domain binding protein 4	3
6827	SUPT4H1	SPT4 homolog, DSIF elongation factor subunit	3
116224	FAM122A	family with sequence similarity 122A	3

51110	LACTB2	lactamase beta 2	3
29063	ZCCHC4	zinc finger CCHC-type containing 4	3
57552	NCEH1	neutral cholesterol ester hydrolase 1	3
60528	ELAC2	elaC ribonuclease Z 2	3
79174	CRELD2	cysteine rich with EGF like domains 2	3
83940	TATDN1	TatD DNase domain containing 1	3
117246	FTSJ3	FtsJ homolog 3	3
390916	NUDT19	nudix hydrolase 19	3
1478	CSTF2	cleavage stimulation factor subunit 2	3
1017	CDK2	cyclin dependent kinase 2	3
221830	TWISTNB	TWIST neighbor	3
10383	TUBB4B	tubulin beta 4B class IVb	3
65003	MRPL11	mitochondrial ribosomal protein L11	3
5366	PMAIP1	phorbol-12-myristate-13-acetate-induced protein 1	3
54939	COMMD4	COMM domain containing 4	3
56912	IFT46	intraflagellar transport 46	3
51258	MRPL51	mitochondrial ribosomal protein L51	3
6478	SIAH2	siah E3 ubiquitin protein ligase 2	3
29093	MRPL22	mitochondrial ribosomal protein L22	3
79073	TMEM109	transmembrane protein 109	3
92745	SLC38A5	solute carrier family 38 member 5	3
9183	ZW10	zw10 kinetochore protein	3
6390	SDHB	succinate dehydrogenase complex iron sulfur subunit B	3
64223	MLST8	MTOR associated protein, LST8 homolog	3
55915	LANCL2	LanC like 2	3
57095	PITHD1	PITH domain containing 1	3
7917	BAG6	BCL2 associated athanogene 6	3
1603	DAD1	defender against cell death 1	3
533	ATP6V0B	ATPase H+ transporting V0 subunit b	3
130355	C2orf76	chromosome 2 open reading frame 76	3
9040	UBE2M	ubiquitin conjugating enzyme E2 M	3
5708	PSMD2	proteasome 26S subunit, non-ATPase 2	3
253714	MMS22L	MMS22 like, DNA repair protein	3
5685	PSMA4	proteasome subunit alpha 4	3
5203	PFDN4	prefoldin subunit 4	3
1376	CPT2	carnitine palmitoyltransferase 2	3
27229	TUBGCP4	tubulin gamma complex associated protein 4	3
83746	L3MBTL2	L3MBTL2 polycomb repressive complex 1 subunit	3
334	APLP2	amyloid beta precursor like protein 2	3
1737	DLAT	dihydrolipoamide S-acetyltransferase	3
5034	P4HB	prolyl 4-hydroxylase subunit beta	3
51053	GMNN	geminin, DNA replication inhibitor	3
51728	POLR3K	RNA polymerase III subunit K	3
116138	KLHDC3	kelch domain containing 3	3
27249	MMADHC	methylmalonic aciduria and homocystinuria, cblD type	3
57019	CIAPIN1	cytokine induced apoptosis inhibitor 1	3
81037	CLPTM1L	CLPTM1 like	3
9862	MED24	mediator complex subunit 24	3
580	BARD1	BRCA1 associated RING domain 1	3
9703	KIAA0100	KIAA0100	3
9538	EI24	EI24, autophagy associated transmembrane protein	3
28957	MRPS28	mitochondrial ribosomal protein S28	3
23534	TNPO3	transportin 3	3
54471	MIEF1	mitochondrial elongation factor 1	3
51264	MRPL27	mitochondrial ribosomal protein L27	3
689	BTF3	basic transcription factor 3	3
7982	ST7	suppression of tumorigenicity 7	3
5984	RFC4	replication factor C subunit 4	3
81875	ISG20L2	interferon stimulated exonuclease gene 20 like 2	3
80010	RMI1	RecQ mediated genome instability 1	3
127253	TYW3	tRNA-yW synthesizing protein 3 homolog	3
8607	RUVBL1	RuvB like AAA ATPase 1	3
10971	YWHAQ	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein theta	3
51253	MRPL37	mitochondrial ribosomal protein L37	3

740	MRPL49	mitochondrial ribosomal protein L49	3
92399	MRRF	mitochondrial ribosome recycling factor	3
6941	TCF19	transcription factor 19	3
4176	MCM7	minichromosome maintenance complex component 7	3
79751	SLC25A22	solute carrier family 25 member 22	3
129401	NUP35	nucleoporin 35	3
4085	MAD2L1	MAD2 mitotic arrest deficient-like 1 (yeast)	3
79892	MCMBP	minichromosome maintenance complex binding protein	3
7705	ZNF146	zinc finger protein 146	3
10857	PGRMC1	progesterone receptor membrane component 1	3
140707	BRI3BP	BRI3 binding protein	3
84798	C19orf48	chromosome 19 open reading frame 48	3
4733	DRG1	developmentally regulated GTP binding protein 1	3
3458	IFNG	interferon gamma	3
7124	TNF	tumor necrosis factor	3
60678	EEFSEC	eukaryotic elongation factor, selenocysteine-tRNA specific	3
55706	NDC1	NDC1 transmembrane nucleoporin	3
56006	SMG9	SMG9, nonsense mediated mRNA decay factor	3
1437	CSF2	colony stimulating factor 2	3
9093	DNAJA3	DnaJ heat shock protein family (Hsp40) member A3	3
55536	CDCA7L	cell division cycle associated 7 like	3
23594	ORC6	origin recognition complex subunit 6	3
81611	ANP32E	acidic nuclear phosphoprotein 32 family member E	3
55166	CENPQ	centromere protein Q	3
90121	TSR2	TSR2, ribosome maturation factor	3
64795	RMND5A	required for meiotic nuclear division 5 homolog A	3
2187	FANCB	Fanconi anemia complementation group B	3
3595	IL12RB2	interleukin 12 receptor subunit beta 2	3
2747	GLUD2	glutamate dehydrogenase 2	3
57001	SDHAF3	succinate dehydrogenase complex assembly factor 3	3
10714	POLD3	DNA polymerase delta 3, accessory subunit	3
51522	TMEM14C	transmembrane protein 14C	3
8841	HDAC3	histone deacetylase 3	3
134145	FAM173B	family with sequence similarity 173 member B	3
10527	IPO7	importin 7	3
10768	AHCYL1	adenosylhomocysteinase like 1	3
29851	ICOS	inducible T-cell costimulator	3
5433	POLR2D	RNA polymerase II subunit D	3
9533	POLR1C	RNA polymerase I subunit C	3
54675	CRLS1	cardiolipin synthase 1	3
145173	B3GLCT	beta 3-glucosyltransferase	3
57602	USP36	ubiquitin specific peptidase 36	3
9801	MRPL19	mitochondrial ribosomal protein L19	3
10539	GLRX3	glutaredoxin 3	3
10921	RNPS1	RNA binding protein with serine rich domain 1	3
92856	IMP4	IMP4 homolog, U3 small nucleolar ribonucleoprotein	3
5810	RAD1	RAD1 checkpoint DNA exonuclease	3
10797	MTHFD2	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase	3
55735	DNAJC11	DnaJ heat shock protein family (Hsp40) member C11	3
10713	USP39	ubiquitin specific peptidase 39	3
81929	SEH1L	SEH1 like nucleoporin	3
5717	PSMD11	proteasome 26S subunit, non-ATPase 11	3
5917	RARS	arginyl-tRNA synthetase	3
27258	LSM3	LSM3 homolog, U6 small nuclear RNA and mRNA degradation associated	3
51182	HSPA14	heat shock protein family A (Hsp70) member 14	3
6950	TCP1	t-complex 1	3
5860	QDPR	quinoid dihydropteridine reductase	3
8079	MLF2	myeloid leukemia factor 2	3
51645	PPIL1	peptidylprolyl isomerase like 1	3
5985	RFC5	replication factor C subunit 5	3
3843	IPO5	importin 5	3
22936	ELL2	elongation factor for RNA polymerase II 2	3
10166	SLC25A15	solute carrier family 25 member 15	3
55622	TTC27	tetratricopeptide repeat domain 27	3

51002	TPRKB	TP53RK binding protein	3
23392	KIAA0368	KIAA0368	3
53407	STX18	syntaxin 18	3
10059	DNM1L	dynamin 1 like	3
9774	BCLAF1	BCL2 associated transcription factor 1	3
84641	MFSD14B	major facilitator superfamily domain containing 14B	3
8677	STX10	syntaxin 10	3
81873	ARPC5L	actin related protein 2/3 complex subunit 5 like	3
51575	ESF1	ESF1 nucleolar pre-rRNA processing protein homolog	3
988	CDC5L	cell division cycle 5 like	3
2957	GTF2A1	general transcription factor IIA subunit 1	3
23597	ACOT9	acyl-CoA thioesterase 9	3
81554	RCC1L	RCC1 like	3
3654	IRAK1	interleukin 1 receptor associated kinase 1	3
55149	MTPAP	mitochondrial poly(A) polymerase	3
80775	TMEM177	transmembrane protein 177	3
64216	TFB2M	transcription factor B2, mitochondrial	3
10592	SMC2	structural maintenance of chromosomes 2	3
140735	DYNLL2	dynein light chain LC8-type 2	3
47	ACLY	ATP citrate lyase	3
5832	ALDH18A1	aldehyde dehydrogenase 18 family member A1	3
1138	CHRNA5	cholinergic receptor nicotinic alpha 5 subunit	3
125228	FAM210A	family with sequence similarity 210 member A	3
23649	POLA2	DNA polymerase alpha 2, accessory subunit	3
55627	SMPD4	sphingomyelin phosphodiesterase 4	3
6510	SLC1A5	solute carrier family 1 member 5	3
58478	ENOPH1	enolase-phosphatase 1	3
2806	GOT2	glutamic-oxaloacetic transaminase 2	3
5534	PPP3R1	protein phosphatase 3 regulatory subunit B, alpha	3
88745	RRP36	ribosomal RNA processing 36	3
79863	RBFA	ribosome binding factor A (putative)	3
10884	MRPS30	mitochondrial ribosomal protein S30	3
9015	TAF1A	TATA-box binding protein associated factor, RNA polymerase I subunit A	3
79029	SPATA5L1	spermatogenesis associated 5 like 1	3
80311	KLHL15	kelch like family member 15	3
64946	CENPH	centromere protein H	3
8438	RAD54L	RAD54-like (S. cerevisiae)	3
7298	TYMS	thymidylate synthetase	3
9768	KIAA0101	KIAA0101	3
6502	SKP2	S-phase kinase associated protein 2	3
5427	POLE2	DNA polymerase epsilon 2, accessory subunit	3
79902	NUP85	nucleoporin 85	3
8723	SNX4	sorting nexin 4	3
5932	RBBP8	RB binding protein 8, endonuclease	3
3070	HELLS	helicase, lymphoid-specific	3
672	BRCA1	BRCA1, DNA repair associated	3
79075	DSCC1	DNA replication and sister chromatid cohesion 1	3
7083	TK1	thymidine kinase 1	3
91768	CABLES1	Cdk5 and Abl enzyme substrate 1	3
10099	TSPAN3	tetraspanin 3	3
130074	FAM168B	family with sequence similarity 168 member B	3
79807	GSTCD	glutathione S-transferase C-terminal domain containing	3
83480	PUS3	pseudouridylate synthase 3	3
54442	KCTD5	potassium channel tetramerization domain containing 5	3
55559	HAUS7	HAUS augmin like complex subunit 7	3
79003	MIS12	MIS12, kinetochore complex component	3
1763	DNA2	DNA replication helicase/nuclease 2	3
9328	GTF3C5	general transcription factor IIIC subunit 5	3
10552	ARPC1A	actin related protein 2/3 complex subunit 1A	3
29925	GMPPB	GDP-mannose pyrophosphorylase B	3
134353	LSM11	LSM11, U7 small nuclear RNA associated	3
25914	RTTN	rotatin	3
207	AKT1	AKT serine/threonine kinase 1	3
64837	KLC2	kinesin light chain 2	3

8131	NPRL3	NPR3 like, GATOR1 complex subunit	3
116113	FOXP4	forkhead box P4	3
55677	IWS1	IWS1, SUPT6H interacting protein	3
10749	KIF1C	kinesin family member 1C	3
9019	MPZL1	myelin protein zero like 1	3
84885	ZDHHC12	zinc finger DHHC-type containing 12	3
55509	BATF3	basic leucine zipper ATF-like transcription factor 3	3
54976	C20orf27	chromosome 20 open reading frame 27	3
56616	DIABLO	diablo IAP-binding mitochondrial protein	3
10856	RUVBL2	RuvB like AAA ATPase 2	3
55969	C20orf24	chromosome 20 open reading frame 24	3
100506012	PPP5D1	PPP5 tetratricopeptide repeat domain containing 1	3
57418	WDR18	WD repeat domain 18	3
10572	SIVA1	SIVA1 apoptosis inducing factor	3
9653	HS2ST1	heparan sulfate 2-O-sulfotransferase 1	3
9031	BAZ1B	bromodomain adjacent to zinc finger domain 1B	3
55922	NKRF	NFKB repressing factor	3
10594	PRPF8	pre-mRNA processing factor 8	3
2235	FECH	ferrochelatase	3
54934	KANSL2	KAT8 regulatory NSL complex subunit 2	3
339231	ARL16	ADP ribosylation factor like GTPase 16	3
5514	PPP1R10	protein phosphatase 1 regulatory subunit 10	3
4193	MDM2	MDM2 proto-oncogene	3
126731	CCSAP	centriole, cilia and spindle associated protein	3
387338	NSUN4	NOP2/Sun RNA methyltransferase family member 4	3
64318	NOC3L	NOC3 like DNA replication regulator	3
64083	GOLPH3	golgi phosphoprotein 3	3
10478	SLC25A17	solute carrier family 25 member 17	3
11157	LSM6	LSM6 homolog, U6 small nuclear RNA and mRNA degradation associated	3
79989	TTC26	tetratricopeptide repeat domain 26	3
56894	AGPAT3	1-acylglycerol-3-phosphate O-acyltransferase 3	3
1983	EIF5	eukaryotic translation initiation factor 5	3
56652	C10orf2	chromosome 10 open reading frame 2	3
22891	ZNF365	zinc finger protein 365	3
221035	REEP3	receptor accessory protein 3	3
54707	GPN2	GPN-loop GTPase 2	3
51022	GLRX2	glutaredoxin 2	3
79066	METTL16	methyltransferase like 16	3
57862	ZNF410	zinc finger protein 410	3
9240	PNMA1	paraneoplastic Ma antigen 1	3
51204	TACO1	translational activator of cytochrome c oxidase I	3
7292	TNFSF4	tumor necrosis factor superfamily member 4	3
79568	C2orf47	chromosome 2 open reading frame 47	3
7584	ZNF35	zinc finger protein 35	3
4709	NDUFB3	NADH:ubiquinone oxidoreductase subunit B3	3
55572	FOXRED1	FAD dependent oxidoreductase domain containing 1	3
56683	C21orf59	chromosome 21 open reading frame 59	3
23423	TMED3	transmembrane p24 trafficking protein 3	3
5134	PDCD2	programmed cell death 2	3
84289	ING5	inhibitor of growth family member 5	3
527	ATP6V0C	ATPase H+ transporting V0 subunit c	3
1978	EIF4EBP1	eukaryotic translation initiation factor 4E binding protein 1	3
6628	SNRPB	small nuclear ribonucleoprotein polypeptides B and B1	3
1981	EIF4G1	eukaryotic translation initiation factor 4 gamma 1	3
10221	TRIB1	tribbles pseudokinase 1	3
157506	RDH10	retinol dehydrogenase 10 (all-trans)	3
79413	ZBED2	zinc finger BED-type containing 2	3
6182	MRPL12	mitochondrial ribosomal protein L12	3
201514	ZNF584	zinc finger protein 584	3
7023	TFAP4	transcription factor AP-4	3
8228	PNPLA4	patatin like phospholipase domain containing 4	3
2593	GAMT	guanidinoacetate N-methyltransferase	3
9144	SYNGR2	synaptogyrin 2	3
2876	GPX1	glutathione peroxidase 1	3
29914	UBIAD1	UbiA prenyltransferase domain containing 1	3

5050	PAFAH1B3	platelet activating factor acetylhydrolase 1b catalytic subunit 3	3
23276	KLHL18	kelch like family member 18	3
51647	FAM96B	family with sequence similarity 96 member B	3
23381	SMG5	SMG5, nonsense mediated mRNA decay factor	3
5714	PSMD8	proteasome 26S subunit, non-ATPase 8	3
4946	OAZ1	ornithine decarboxylase antizyme 1	3
6647	SOD1	superoxide dismutase 1, soluble	3
4234	METTL1	methyltransferase like 1	3
116238	TLCD1	TLC domain containing 1	3
7167	TPI1	triosephosphate isomerase 1	3
10953	TOMM34	translocase of outer mitochondrial membrane 34	3
27341	RRP7A	ribosomal RNA processing 7 homolog A	3
65057	ACD	adrenocortical dysplasia homolog	3
64943	NT5DC2	5'-nucleotidase domain containing 2	3
5425	POLD2	DNA polymerase delta 2, accessory subunit	3
79143	MBOAT7	membrane bound O-acyltransferase domain containing 7	3
9361	LONP1	lon peptidase 1, mitochondrial	3
6150	MRPL23	mitochondrial ribosomal protein L23	3
1337	COX6A1	cytochrome c oxidase subunit 6A1	3
10726	NUDC	nuclear distribution C, dynein complex regulator	3
51690	LSM7	LSM7 homolog, U6 small nuclear RNA and mRNA degradation associated	3
5441	POLR2L	RNA polymerase II subunit L	3
55272	IMP3	IMP3, U3 small nucleolar ribonucleoprotein	3
11047	ADRM1	adhesion regulating molecule 1	3
23170	TTLL12	tubulin tyrosine ligase like 12	3
53354	PANK1	pantothenate kinase 1	3
3692	EIF6	eukaryotic translation initiation factor 6	3
5709	PSMD3	proteasome 26S subunit, non-ATPase 3	3
23543	RBFOX2	RNA binding protein, fox-1 homolog 2	3
56834	GPR137	G protein-coupled receptor 137	3
8402	SLC25A11	solute carrier family 25 member 11	3
5694	PSMB6	proteasome subunit beta 6	3
10113	PREB	prolactin regulatory element binding	3
26073	POLDIP2	DNA polymerase delta interacting protein 2	3
28989	NTMT1	N-terminal Xaa-Pro-Lys N-methyltransferase 1	3
55856	ACOT13	acyl-CoA thioesterase 13	3
29934	SNX12	sorting nexin 12	3
23645	PPP1R15A	protein phosphatase 1 regulatory subunit 15A	3
51278	IER5	immediate early response 5	3
10063	COX17	COX17, cytochrome c oxidase copper chaperone	3
83706	FERMT3	fermitin family member 3	3
54973	CPSF3L	cleavage and polyadenylation specific factor 3-like	3
401466	C8orf59	chromosome 8 open reading frame 59	3
84287	ZDHHC16	zinc finger DHHC-type containing 16	3
10257	ABCC4	ATP binding cassette subfamily C member 4	3
23466	CBX6	chromobox 6	3
64965	MRPS9	mitochondrial ribosomal protein S9	3
51097	SCCPDH	saccharopine dehydrogenase (putative)	3
51659	GINS2	GINS complex subunit 2	3
6434	TRA2B	transformer 2 beta homolog (Drosophila)	3
471	ATIC	5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase/IMP cyclohydrolase	3
23074	UHRF1BP1L	UHRF1 binding protein 1 like	3
10598	AHSA1	activator of Hsp90 ATPase activity 1	3
1653	DDX1	DEAD/H-box helicase 1	3
57695	USP37	ubiquitin specific peptidase 37	3
3840	KPNA4	karyopherin subunit alpha 4	3
54517	PUS7	pseudouridylate synthase 7 (putative)	3
8870	IER3	immediate early response 3	3
9761	MLEC	malectin	3
116225	ZMYND19	zinc finger MYND-type containing 19	3
6183	MRPS12	mitochondrial ribosomal protein S12	3
9308	CD83	CD83 molecule	3
10061	ABCF2	ATP binding cassette subfamily F member 2	3
6484	ST3GAL4	ST3 beta-galactoside alpha-2,3-sialyltransferase 4	3

283742	FAM98B	family with sequence similarity 98 member B	3
27158	NDOR1	NADPH dependent diflavin oxidoreductase 1	3
126792	B3GALT6	beta-1,3-galactosyltransferase 6	3
51400	PPME1	protein phosphatase methylesterase 1	3
10694	CCT8	chaperonin containing TCP1 subunit 8	3
29090	TIMM21	translocase of inner mitochondrial membrane 21	3
4670	HNRNPM	heterogeneous nuclear ribonucleoprotein M	3
10988	METAP2	methionyl aminopeptidase 2	3
9868	TOMM70	translocase of outer mitochondrial membrane 70	3
1431	CS	citrate synthase	3
3157	HMGCS1	3-hydroxy-3-methylglutaryl-CoA synthase 1	3
11112	HIBADH	3-hydroxyisobutyrate dehydrogenase	3
10213	PSMD14	proteasome 26S subunit, non-ATPase 14	3
1434	CSE1L	chromosome segregation 1 like	3
51081	MRPS7	mitochondrial ribosomal protein S7	3
23590	PDSS1	prenyl (decaprenyl) diphosphate synthase, subunit 1	3
6749	SSRP1	structure specific recognition protein 1	3
3562	IL3	interleukin 3	3
10189	ALYREF	Aly/REF export factor	3
6431	SRSF6	serine and arginine rich splicing factor 6	3
292	SLC25A5	solute carrier family 25 member 5	3
23160	WDR43	WD repeat domain 43	3
2030	SLC29A1	solute carrier family 29 member 1 (Augustine blood group)	3
5536	PPP5C	protein phosphatase 5 catalytic subunit	3
9188	DDX21	DEAD-box helicase 21	3
8726	EED	embryonic ectoderm development	3
29889	GNL2	G protein nucleolar 2	3
4436	MSH2	mutS homolog 2	3
4175	MCM6	minichromosome maintenance complex component 6	3
10939	AFG3L2	AFG3 like matrix AAA peptidase subunit 2	3
1994	ELAVL1	ELAV like RNA binding protein 1	3
23450	SF3B3	splicing factor 3b subunit 3	3
29781	NCAPH2	non-SMC condensin II complex subunit H2	3
5707	PSMD1	proteasome 26S subunit, non-ATPase 1	3
10657	KHDRBS1	KH RNA binding domain containing, signal transduction associated 1	3
10432	RBM14	RNA binding motif protein 14	3
7518	XRCC4	X-ray repair cross complementing 4	3
3301	DNAJA1	DnaJ heat shock protein family (Hsp40) member A1	3
2935	GSPT1	G1 to S phase transition 1	3
1982	EIF4G2	eukaryotic translation initiation factor 4 gamma 2	3
3184	HNRNPD	heterogeneous nuclear ribonucleoprotein D	3
23082	PPRC1	peroxisome proliferator-activated receptor gamma, coactivator-related 1	3
27089	UQCRQ	ubiquinol-cytochrome c reductase complex III subunit VII	3
7165	TPD52L2	tumor protein D52 like 2	3
29098	RANGRF	RAN guanine nucleotide release factor	3
8260	NAA10	N(alpha)-acetyltransferase 10, NatA catalytic subunit	3
51373	MRPS17	mitochondrial ribosomal protein S17	3
1892	ECHS1	enoyl-CoA hydratase, short chain 1	3
22868	FASTKD2	FAST kinase domains 2	3
5931	RBBP7	RB binding protein 7, chromatin remodeling factor	3
84135	UTP15	UTP15, small subunit processome component	3
23165	NUP205	nucleoporin 205	3
5202	PFDN2	prefoldin subunit 2	3
84331	MCRIP2	MAPK regulated corepressor interacting protein 2	3
705	BYSL	bystin like	3
3622	ING2	inhibitor of growth family member 2	3
9631	NUP155	nucleoporin 155	3
79711	IPO4	importin 4	3
1660	DHX9	DEAH-box helicase 9	3
7372	UMPS	uridine monophosphate synthetase	3
199953	TMEM201	transmembrane protein 201	3
3068	HDGF	hepatoma-derived growth factor	3
10295	BCKDK	branched chain ketoacid dehydrogenase kinase	3
144097	C11orf84	chromosome 11 open reading frame 84	3
4628	MYH10	myosin heavy chain 10	3
84649	DGAT2	diacylglycerol O-acyltransferase 2	3

516	ATP5G1	ATP synthase, H+ transporting, mitochondrial Fo complex subunit C1 (subunit 9)	3
5719	PSMD13	proteasome 26S subunit, non-ATPase 13	3
1212	CLTB	clathrin light chain B	3
8882	ZPR1	ZPR1 zinc finger	3
10430	TMEM147	transmembrane protein 147	3
10534	SSSCA1	Sjogren syndrome/scleroderma autoantigen 1	3
8664	EIF3D	eukaryotic translation initiation factor 3 subunit D	3
79572	ATP13A3	ATPase 13A3	3
10452	TOMM40	translocase of outer mitochondrial membrane 40	3
3615	IMPDH2	inosine monophosphate dehydrogenase 2	3
85476	GFM1	G elongation factor mitochondrial 1	3
10575	CCT4	chaperonin containing TCP1 subunit 4	3
2184	FAH	fumarylacetoacetate hydrolase	3
201161	CENPV	centromere protein V	3
121053	C12orf45	chromosome 12 open reading frame 45	3
5198	PFAS	phosphoribosylformylglycinamidine synthase	3
113419	TEX261	testis expressed 261	3
3308	HSPA4	heat shock protein family A (Hsp70) member 4	3
9654	TTLL4	tubulin tyrosine ligase like 4	3
23	ABCF1	ATP binding cassette subfamily F member 1	3
4171	MCM2	minichromosome maintenance complex component 2	3
9929	JOSD1	Josephin domain containing 1	3
949	SCARB1	scavenger receptor class B member 1	3
192111	PGAM5	PGAM family member 5, mitochondrial serine/threonine protein phosphatase	3
23277	CLUH	clustered mitochondria homolog	3
27042	DIEXF	digestive organ expansion factor homolog (zebrafish)	3
10155	TRIM28	tripartite motif containing 28	3
54919	DNAAF5	dynein axonemal assembly factor 5	3
7517	XRCC3	X-ray repair cross complementing 3	3
4174	MCM5	minichromosome maintenance complex component 5	3
84817	TXNDC17	thioredoxin domain containing 17	3
5434	POLR2E	RNA polymerase II subunit E	3
9146	HGS	hepatocyte growth factor-regulated tyrosine kinase substrate	3
79709	COLGALT1	collagen beta(1-O)galactosyltransferase 1	3
2802	GOLGA3	golgin A3	3
2706	GJB2	gap junction protein beta 2	3
55120	FANCL	Fanconi anemia complementation group L	3
25885	POLR1A	RNA polymerase I subunit A	3
54107	POLE3	DNA polymerase epsilon 3, accessory subunit	3
57464	STRIP2	striatin interacting protein 2	3
1848	DUSP6	dual specificity phosphatase 6	3
154807	VKORC1L1	vitamin K epoxide reductase complex subunit 1 like 1	3
127396	ZNF684	zinc finger protein 684	3
222229	LRWD1	leucine rich repeats and WD repeat domain containing 1	3
351	APP	amyloid beta precursor protein	3
63932	CXorf56	chromosome X open reading frame 56	3
65108	MARCKSL1	MARCKS like 1	3
23413	NCS1	neuronal calcium sensor 1	3
2963	GTF2F2	general transcription factor IIF subunit 2	3
548645	DNAJC25	DnaJ heat shock protein family (Hsp40) member C25	3
56655	POLE4	DNA polymerase epsilon 4, accessory subunit	3
7532	YWHAG	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein gamma	3
84326	METTL26	methyltransferase like 26	3
51259	TMEM216	transmembrane protein 216	3
8662	EIF3B	eukaryotic translation initiation factor 3 subunit B	3
14	AAMP	angio associated migratory cell protein	3
29893	PSMC3IP	PSMC3 interacting protein	3
55142	HAUS2	HAUS augmin like complex subunit 2	3
10204	NUTF2	nuclear transport factor 2	3
81620	CDT1	chromatin licensing and DNA replication factor 1	3
11072	DUSP14	dual specificity phosphatase 14	3
10538	BATF	basic leucine zipper ATF-like transcription factor	3
1022	CDK7	cyclin dependent kinase 7	3
79080	CCDC86	coiled-coil domain containing 86	3
64979	MRPL36	mitochondrial ribosomal protein L36	3

112812	FDX1L	ferredoxin 1 like	3
1642	DDB1	damage specific DNA binding protein 1	3
84262	PSMG3	proteasome assembly chaperone 3	3
55862	ECHDC1	ethylmalonyl-CoA decarboxylase 1	3
64785	GINS3	GINS complex subunit 3	3
5438	POLR2I	RNA polymerase II subunit I	3
286	ANK1	ankyrin 1	3
51534	VTA1	vesicle trafficking 1	3
2717	GLA	galactosidase alpha	3
84916	UTP4	UTP4, small subunit processome component	3
64963	MRPS11	mitochondrial ribosomal protein S11	3
6351	CCL4	C-C motif chemokine ligand 4	3
79022	TMEM106C	transmembrane protein 106C	3
8395	PIP5K1B	phosphatidylinositol-4-phosphate 5-kinase type 1 beta	3
4809	SNU13	SNU13 homolog, small nuclear ribonucleoprotein (U4/U6.U5)	3
60673	ATG101	autophagy related 101	3
29105	CFAP20	cilia and flagella associated protein 20	3
114971	PTPMT1	protein tyrosine phosphatase, mitochondrial 1	3
27020	NPTN	neuroplastin	3
10248	POP7	POP7 homolog, ribonuclease P/MRP subunit	3
9775	EIF4A3	eukaryotic translation initiation factor 4A3	3
79155	TNIP2	TNFAIP3 interacting protein 2	3
1211	CLTA	clathrin light chain A	3
5693	PSMB5	proteasome subunit beta 5	3
7262	PHLDA2	pleckstrin homology like domain family A member 2	3
131566	DCBLD2	discoidin, CUB and LCCL domain containing 2	3
29902	FAM216A	family with sequence similarity 216 member A	3
51013	EXOSC1	exosome component 1	3
27309	ZNF330	zinc finger protein 330	3
64983	MRPL32	mitochondrial ribosomal protein L32	3
5036	PA2G4	proliferation-associated 2G4	3
51010	EXOSC3	exosome component 3	3
147184	TMEM99	transmembrane protein 99	3
60314	C12orf10	chromosome 12 open reading frame 10	3
79590	MRPL24	mitochondrial ribosomal protein L24	3
154467	CCDC167	coiled-coil domain containing 167	3
483	ATP1B3	ATPase Na+/K+ transporting subunit beta 3	3
282991	BLOC1S2	biogenesis of lysosomal organelles complex 1 subunit 2	3
10322	SMYD5	SMYD family member 5	3
4000	LMNA	lamin A/C	3
1497	CTNS	cystinosin, lysosomal cystine transporter	3
51073	MRPL4	mitochondrial ribosomal protein L4	3
6449	SGTA	small glutamine rich tetratricopeptide repeat containing alpha	3
10186	LHFP	lipoma HMGIC fusion partner	3
55847	CISD1	CDGSH iron sulfur domain 1	3
25940	FAM98A	family with sequence similarity 98 member A	3
9861	PSMD6	proteasome 26S subunit, non-ATPase 6	3
356	FASLG	Fas ligand	3
79077	DCTPP1	dCTP pyrophosphatase 1	3
57514	ARHGAP31	Rho GTPase activating protein 31	3
84259	DCUN1D5	defective in cullin neddylation 1 domain containing 5	3
1104	RCC1	regulator of chromosome condensation 1	3
54555	DDX49	DEAD-box helicase 49	3
84769	MPV17L2	MPV17 mitochondrial inner membrane protein like 2	3
119559	SFXN4	sideroflexin 4	3
55968	NSFL1C	NSFL1 cofactor	3
3066	HDAC2	histone deacetylase 2	3
1984	EIF5A	eukaryotic translation initiation factor 5A	3
4792	NFKBIA	NFKB inhibitor alpha	3
7314	UBB	ubiquitin B	3
5704	PSMC4	proteasome 26S subunit, ATPase 4	3
125144	LRRC75A-AS1	LRRC75A antisense RNA 1	3
50486	G0S2	G0/G1 switch 2	3
54955	C1orf109	chromosome 1 open reading frame 109	3
25804	LSM4	LSM4 homolog, U6 small nuclear RNA and mRNA degradation associated	3

51021	MRPS16	mitochondrial ribosomal protein S16	3
54475	NLE1	notchless homolog 1	3
56915	EXOSC5	exosome component 5	3
92579	G6PC3	glucose-6-phosphatase catalytic subunit 3	3
2590	GALNT2	polypeptide N-acetylgalactosaminyltransferase 2	3
54663	WDR74	WD repeat domain 74	3
4201	MEA1	male-enhanced antigen 1	3
3558	IL2	interleukin 2	3
5250	SLC25A3	solute carrier family 25 member 3	3
1844	DUSP2	dual specificity phosphatase 2	3
5326	PLAGL2	PLAG1 like zinc finger 2	3
83596	BCL2L12	BCL2 like 12	3
84285	EIF1AD	eukaryotic translation initiation factor 1A domain containing	3
5245	PHB	prohibitin	3
27351	DESI1	desumoylating isopeptidase 1	3
5902	RANBP1	RAN binding protein 1	3
54982	CLN6	ceroid-lipofuscinosis, neuronal 6, late infantile, variant	3
5725	PTBP1	polypyrimidine tract binding protein 1	3
30000	TNPO2	transportin 2	3
51144	HSD17B12	hydroxysteroid 17-beta dehydrogenase 12	3
5552	SRGN	serglycin	3
5251	PHEX	phosphate regulating endopeptidase homolog, X-linked	3
4953	ODC1	ornithine decarboxylase 1	3
8740	TNFSF14	tumor necrosis factor superfamily member 14	3
6723	SRM	spermidine synthase	3
55352	COPRS	coordinator of PRMT5 and differentiation stimulator	3
7866	IFRD2	interferon related developmental regulator 2	3
23076	RRP1B	ribosomal RNA processing 1B	3
112464	PRKCDBP	protein kinase C delta binding protein	3
66005	CHID1	chitinase domain containing 1	3
388962	BOLA3	bolA family member 3	3
7293	TNFRSF4	TNF receptor superfamily member 4	3
4927	NUP88	nucleoporin 88	3
3002	GZMB	granzyme B	3
3559	IL2RA	interleukin 2 receptor subunit alpha	3
79033	ERI3	ERI1 exoribonuclease family member 3	3
494143	CHAC2	ChaC cation transport regulator homolog 2	3
84833	USMG5	up-regulated during skeletal muscle growth 5 homolog (mouse)	3
7283	TUBG1	tubulin gamma 1	3
51371	POMP	proteasome maturation protein	3
51605	TRMT6	tRNA methyltransferase 6	3
54865	GPATCH4	G-patch domain containing 4	3
219927	MRPL21	mitochondrial ribosomal protein L21	3
2091	FBL	fibrillarin	3
5695	PSMB7	proteasome subunit beta 7	3
1460	CSNK2B	casein kinase 2 beta	3
7965	AIMP2	aminoacyl tRNA synthetase complex interacting multifunctional protein 2	3
200916	RPL22L1	ribosomal protein L22 like 1	3
4700	NDUFA6	NADH:ubiquinone oxidoreductase subunit A6	3
10549	PRDX4	peroxiredoxin 4	3
84807	NFKBID	NFKB inhibitor delta	3
2288	FKBP4	FK506 binding protein 4	3
3276	PRMT1	protein arginine methyltransferase 1	3
60488	MRPS35	mitochondrial ribosomal protein S35	3
23481	PES1	pescadillo ribosomal biogenesis factor 1	3
196383	RILPL2	Rab interacting lysosomal protein like 2	3
2224	FDPS	farnesyl diphosphate synthase	3
55003	PAK1IP1	PAK1 interacting protein 1	3
126382	NR2C2AP	nuclear receptor 2C2 associated protein	3
51504	TRMT112	tRNA methyltransferase 11-2 homolog (S. cerevisiae)	3
92609	TIMM50	translocase of inner mitochondrial membrane 50	3
708	C1QBP	complement C1q binding protein	3
10327	AKR1A1	aldo-keto reductase family 1 member A1	3
6921	TCEB1	transcription elongation factor B subunit 1	3
26517	TIMM13	translocase of inner mitochondrial membrane 13	3

84313	VPS25	vacuolar protein sorting 25 homolog	3
63875	MRPL17	mitochondrial ribosomal protein L17	3
5435	POLR2F	RNA polymerase II subunit F	3
79833	GEMIN6	gem nuclear organelle associated protein 6	3
1736	DKC1	dyskerin pseudouridine synthase 1	3
23560	GTPBP4	GTP binding protein 4	3
7371	UCK2	uridine-cytidine kinase 2	3
3182	HNRNPAB	heterogeneous nuclear ribonucleoprotein A/B	3
4691	NCL	nucleolin	3
56902	PNO1	partner of NOB1 homolog	3
3313	HSPA9	heat shock protein family A (Hsp70) member 9	3
1019	CDK4	cyclin dependent kinase 4	3
5901	RAN	RAN, member RAS oncogene family	3
10528	NOP56	NOP56 ribonucleoprotein	3
29015	SLC43A3	solute carrier family 43 member 3	3
25819	NOCT	nocturnin	3
26230	TIAM2	T-cell lymphoma invasion and metastasis 2	3
10969	EBNA1BP2	EBNA1 binding protein 2	3
10135	NAMPT	nicotinamide phosphoribosyltransferase	3
10196	PRMT3	protein arginine methyltransferase 3	3
6626	SNRPA	small nuclear ribonucleoprotein polypeptide A	3
8668	EIF3I	eukaryotic translation initiation factor 3 subunit I	3
113174	SAAL1	serum amyloid A like 1	3
54984	PINX1	PIN2/TERF1 interacting, telomerase inhibitor 1	3
6636	SNRPF	small nuclear ribonucleoprotein polypeptide F	3
5052	PRDX1	peroxiredoxin 1	3
51493	RTCB	RNA 2',3'-cyclic phosphate and 5'-OH ligase	3
3608	ILF2	interleukin enhancer binding factor 2	3
11091	WDR5	WD repeat domain 5	3
10056	FARSB	phenylalanyl-tRNA synthetase beta subunit	3
10492	SYNCRIP	synaptotagmin binding cytoplasmic RNA interacting protein	3
8061	FOSL1	FOS like 1, AP-1 transcription factor subunit	3
3329	HSPD1	heat shock protein family D (Hsp60) member 1	3
9221	NOLC1	nucleolar and coiled-body phosphoprotein 1	3
6631	SNRPC	small nuclear ribonucleoprotein polypeptide C	3
7416	VDAC1	voltage dependent anion channel 1	3
1647	GADD45A	growth arrest and DNA damage inducible alpha	3
3605	IL17A	interleukin 17A	3
617	BCS1L	BCS1 homolog, ubiquinol-cytochrome c reductase complex chaperone	3
93436	ARMC6	armadillo repeat containing 6	3
10227	MFSD10	major facilitator superfamily domain containing 10	3
55624	POMGNT1	protein O-linked mannose N-acetylglucosaminyltransferase 1 (beta 1,2-)	3
64768	IPPK	inositol-pentakisphosphate 2-kinase	3
126321	MFSD12	major facilitator superfamily domain containing 12	3
8192	CLPP	caseinolytic mitochondrial matrix peptidase proteolytic subunit	3
84300	UQCC2	ubiquinol-cytochrome c reductase complex assembly factor 2	3
10244	RABEPK	Rab9 effector protein with kelch motifs	3
57819	LSM2	LSM2 homolog, U6 small nuclear RNA and mRNA degradation associated	3
28958	COA3	cytochrome c oxidase assembly factor 3	3
2109	ETFB	electron transfer flavoprotein beta subunit	3
11266	DUSP12	dual specificity phosphatase 12	3
51474	LIMA1	LIM domain and actin binding 1	3
4731	NDUFV3	NADH:ubiquinone oxidoreductase subunit V3	3
4701	NDUFA7	NADH:ubiquinone oxidoreductase subunit A7	3
9238	TBRG4	transforming growth factor beta regulator 4	3
29080	CCDC59	coiled-coil domain containing 59	3
29985	SLC39A3	solute carrier family 39 member 3	3
1537	CYC1	cytochrome c1	3
8784	TNFRSF18	TNF receptor superfamily member 18	3
9526	MPDU1	mannose-P-dolichol utilization defect 1	3
26121	PRPF31	pre-mRNA processing factor 31	3
977	CD151	CD151 molecule (Raph blood group)	3
83460	EMC6	ER membrane protein complex subunit 6	3
64960	MRPS15	mitochondrial ribosomal protein S15	3
2950	GSTP1	glutathione S-transferase pi 1	3

112939	NACC1	nucleus accumbens associated 1	3
51293	CD320	CD320 molecule	3
5119	CHMP1A	charged multivesicular body protein 1A	3
8886	DDX18	DEAD-box helicase 18	3
8818	DPM2	dolichyl-phosphate mannosyltransferase subunit 2, regulatory	3
26519	TIMM10	translocase of inner mitochondrial membrane 10 homolog (yeast)	3
4236	MFAP1	microfibrillar associated protein 1	3
5214	PFKP	phosphofructokinase, platelet	3
79894	ZNF672	zinc finger protein 672	3
51116	MRPS2	mitochondrial ribosomal protein S2	3
29950	SERTAD1	SERTA domain containing 1	3
23399	CTDNEP1	CTD nuclear envelope phosphatase 1	3
54881	TEX10	testis expressed 10	3
10245	TIMM17B	translocase of inner mitochondrial membrane 17 homolog B (yeast)	3
51236	HGH1	HGH1 homolog	3
55697	VAC14	Vac14, PIKFYVE complex component	3
27183	VPS4A	vacuolar protein sorting 4 homolog A	3
5394	EXOSC10	exosome component 10	3
55157	DARS2	aspartyl-tRNA synthetase 2, mitochondrial	3
3726	JUNB	JunB proto-oncogene, AP-1 transcription factor subunit	3
3281	HSBP1	heat shock factor binding protein 1	3
55658	RNF126	ring finger protein 126	3
9455	HOMER2	homer scaffolding protein 2	3
345630	FBLL1	fibrillarin-like 1	3
29923	HILPDA	hypoxia inducible lipid droplet associated	3
54968	TMEM70	transmembrane protein 70	3
84002	B3GNT5	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5	3
10573	MRPL28	mitochondrial ribosomal protein L28	3
55168	MRPS18A	mitochondrial ribosomal protein S18A	3
4817	NIT1	nitrilase 1	3
7247	TSN	translin	3
54148	MRPL39	mitochondrial ribosomal protein L39	3
29100	TMEM208	transmembrane protein 208	3
9326	ZNHIT3	zinc finger HIT-type containing 3	3
5682	PSMA1	proteasome subunit alpha 1	3
64708	COPS7B	COP9 signalosome subunit 7B	3
6415	SELENOW	selenoprotein W	3
10069	RWDD2B	RWD domain containing 2B	3
54840	APTX	aprataxin	3
112495	GTF3C6	general transcription factor IIIC subunit 6	3
10102	TSFM	Ts translation elongation factor, mitochondrial	3
29097	CNIH4	cornichon family AMPA receptor auxiliary protein 4	3
9391	CIAO1	cytosolic iron-sulfur assembly component 1	3
221143	EEF1AKMT1	eukaryotic translation elongation factor 1 alpha lysine methyltransferase 1	3
4116	MAGOH	mago homolog, exon junction complex core component	3
54887	UHRF1BP1	UHRF1 binding protein 1	3
128553	TSHZ2	teashirt zinc finger homeobox 2	3
9088	PKMYT1	protein kinase, membrane associated tyrosine/threonine 1	3
51154	MRTO4	MRT4 homolog, ribosome maturation factor	3
10131	TRAP1	TNF receptor associated protein 1	3
63933	MCUR1	mitochondrial calcium uniporter regulator 1	3
10212	DDX39A	DEAD-box helicase 39A	3
51714	SELENOT	selenoprotein T	3
4191	MDH2	malate dehydrogenase 2	3
10498	CARM1	coactivator associated arginine methyltransferase 1	3
5817	PVR	poliovirus receptor	3
80764	THAP7	THAP domain containing 7	3
2193	FARSA	phenylalanyl-tRNA synthetase alpha subunit	3
7284	TUFM	Tu translation elongation factor, mitochondrial	3
5426	POLE	DNA polymerase epsilon, catalytic subunit	3
5962	RDX	radixin	3
10785	WDR4	WD repeat domain 4	3
27101	CACYBP	calcyclin binding protein	3
23291	FBXW11	F-box and WD repeat domain containing 11	3
2632	GBE1	1,4-alpha-glucan branching enzyme 1	3

84172	POLR1B	RNA polymerase I subunit B	3
55324	ABCF3	ATP binding cassette subfamily F member 3	3
60625	DHX35	DEAH-box helicase 35	3
8815	BANF1	barrier to autointegration factor 1	3
9937	DCLRE1A	DNA cross-link repair 1A	3
10980	COPS6	COP9 signalosome subunit 6	3
27069	GHITM	growth hormone inducible transmembrane protein	3
2827	GPR3	G protein-coupled receptor 3	3
5432	POLR2C	RNA polymerase II subunit C	3
7458	EIF4H	eukaryotic translation initiation factor 4H	3
51499	TRIAP1	TP53 regulated inhibitor of apoptosis 1	3
5781	PTPN11	protein tyrosine phosphatase, non-receptor type 11	3
53	ACP2	acid phosphatase 2, lysosomal	3
653122	LSM12P1	LSM12 pseudogene 1	3
94081	SFXN1	sideroflexin 1	3
8125	ANP32A	acidic nuclear phosphoprotein 32 family member A	3
3312	HSPA8	heat shock protein family A (Hsp70) member 8	3
54994	GID8	GID complex subunit 8 homolog	3
8898	MTMR2	myotubularin related protein 2	3
5905	RANGAP1	Ran GTPase activating protein 1	3
23141	ANKLE2	ankyrin repeat and LEM domain containing 2	3
196483	EEF2KMT	eukaryotic elongation factor 2 lysine methyltransferase	3
65083	NOL6	nucleolar protein 6	3
51001	MTERF3	mitochondrial transcription termination factor 3	3
51537	MTFP1	mitochondrial fission process 1	3
64065	PERP	PERP, TP53 apoptosis effector	3
6428	SRSF3	serine and arginine rich splicing factor 3	3
60592	SCOC	short coiled-coil protein	3
58477	SRPRB	SRP receptor beta subunit	3
51015	ISOC1	isochorismatase domain containing 1	3
3838	KPNA2	karyopherin subunit alpha 2	3
2553	GABPB1	GA binding protein transcription factor beta subunit 1	3
57486	NLN	neurolysin	3
10130	PDIA6	protein disulfide isomerase family A member 6	3
65008	MRPL1	mitochondrial ribosomal protein L1	3
133957	CCDC127	coiled-coil domain containing 127	3
131474	CHCHD4	coiled-coil-helix-coiled-coil-helix domain containing 4	3
65265	C8orf33	chromosome 8 open reading frame 33	3
10440	TIMM17A	translocase of inner mitochondrial membrane 17 homolog A (yeast)	3
27292	DIMT1	DIM1 dimethyladenosine transferase 1 homolog	3
7336	UBE2V2	ubiquitin conjugating enzyme E2 V2	3
80746	TSEN2	tRNA splicing endonuclease subunit 2	3
8914	TIMELESS	timeless circadian clock	3
2665	GDI2	GDP dissociation inhibitor 2	3
83877	TM2D2	TM2 domain containing 2	3
2618	GART	phosphoribosylglycinamide formyltransferase, phosphoribosylglycinamide synthetase, phosphoribosylaminoimidazole synthetase	3
81034	SLC25A32	solute carrier family 25 member 32	3
29088	MRPL15	mitochondrial ribosomal protein L15	3
56647	BCCIP	BRCA2 and CDKN1A interacting protein	3
10935	PRDX3	peroxiredoxin 3	3
5464	PPA1	pyrophosphatase (inorganic) 1	3
55226	NAT10	N-acetyltransferase 10	3
27349	MCAT	malonyl-CoA-acyl carrier protein transacylase	3
11335	CBX3	chromobox 3	3
1267	CNP	2',3'-cyclic nucleotide 3' phosphodiesterase	3
28998	MRPL13	mitochondrial ribosomal protein L13	3
6945	MLX	MLX, MAX dimerization protein	3
23203	PMPCA	peptidase, mitochondrial processing alpha subunit	3
4190	MDH1	malate dehydrogenase 1	3
84790	TUBA1C	tubulin alpha 1c	3
54997	TESC	tescalcin	3
153443	SRFBP1	serum response factor binding protein 1	3
55164	SHQ1	SHQ1, H/ACA ribonucleoprotein assembly factor	3
8939	FUBP3	far upstream element binding protein 3	3

84991	RBM17	RNA binding motif protein 17	3
26354	GNL3	G protein nucleolar 3	3
84154	RPF2	ribosome production factor 2 homolog	3
10946	SF3A3	splicing factor 3a subunit 3	3
8727	CTNNAL1	catenin alpha like 1	3
100287932	TIMM23	translocase of inner mitochondrial membrane 23	3
7027	TFDP1	transcription factor Dp-1	3
55775	TDP1	tyrosyl-DNA phosphodiesterase 1	3
4723	NDUFV1	NADH:ubiquinone oxidoreductase core subunit V1	3
9352	TXNL1	thioredoxin like 1	3
84541	KBTBD8	kelch repeat and BTB domain containing 8	3
10563	CXCL13	C-X-C motif chemokine ligand 13	3
5796	PTPRK	protein tyrosine phosphatase, receptor type K	3
10940	POP1	POP1 homolog, ribonuclease P/MRP subunit	3
9818	NUP58	nucleoporin 58	3
8602	NOP14	NOP14 nucleolar protein	3
10606	PAICS	phosphoribosylaminoimidazole carboxylase; phosphoribosylaminoimidazolesuccinocarboxamide synthase	3
10963	STIP1	stress induced phosphoprotein 1	3
51018	RRP15	ribosomal RNA processing 15 homolog	3
284098	PIGW	phosphatidylinositol glycan anchor biosynthesis class W	3
8661	EIF3A	eukaryotic translation initiation factor 3 subunit A	3
79731	NARS2	asparaginyl-tRNA synthetase 2, mitochondrial (putative)	3
54806	AHI1	Abelson helper integration site 1	3
55326	AGPAT5	1-acylglycerol-3-phosphate O-acyltransferase 5	3
9277	WDR46	WD repeat domain 46	3
34	ACADM	acyl-CoA dehydrogenase, C-4 to C-12 straight chain	3
9933	PUM3	pumilio RNA binding family member 3	3
3183	HNRNPC	heterogeneous nuclear ribonucleoprotein C (C1/C2)	3
3609	ILF3	interleukin enhancer binding factor 3	3
8847	DLEU2	deleted in lymphocytic leukemia 2 (non-protein coding)	3
84444	DOT1L	DOT1 like histone lysine methyltransferase	3
79728	PALB2	partner and localizer of BRCA2	3
7675	ZNF121	zinc finger protein 121	3
3190	HNRNPK	heterogeneous nuclear ribonucleoprotein K	3
54928	IMPAD1	inositol monophosphatase domain containing 1	3
55055	ZWILCH	zwilch kinetochore protein	3
51649	MRPS23	mitochondrial ribosomal protein S23	3
6432	SRSF7	serine and arginine rich splicing factor 7	3
9689	BZW1	basic leucine zipper and W2 domains 1	3
57122	NUP107	nucleoporin 107	3
55839	CENPN	centromere protein N	3
7337	UBE3A	ubiquitin protein ligase E3A	3
7520	XRCC5	X-ray repair cross complementing 5	3
29843	SENP1	SUMO1/sentrin specific peptidase 1	3
5981	RFC1	replication factor C subunit 1	3
87	ACTN1	actinin alpha 1	3
92162	TMEM88	transmembrane protein 88	3
10951	CBX1	chromobox 1	3
2821	GPI	glucose-6-phosphate isomerase	3
79931	TNIP3	TNFAIP3 interacting protein 3	3
54512	EXOSC4	exosome component 4	3
8682	PEA15	phosphoprotein enriched in astrocytes 15	3
5033	P4HA1	prolyl 4-hydroxylase subunit alpha 1	3
80762	NDFIP1	Nedd4 family interacting protein 1	3
10262	SF3B4	splicing factor 3b subunit 4	3
5230	PGK1	phosphoglycerate kinase 1	3
7334	UBE2N	ubiquitin conjugating enzyme E2 N	3
143279	HECTD2	HECT domain E3 ubiquitin protein ligase 2	3
440093	H3F3C	H3 histone family member 3C	3
760	CA2	carbonic anhydrase 2	3
6621	SNAPC4	small nuclear RNA activating complex polypeptide 4	3
4678	NASP	nuclear autoantigenic sperm protein	3
339448	C1orf174	chromosome 1 open reading frame 174	3
8099	CDK2AP1	cyclin dependent kinase 2 associated protein 1	3

2968	GTF2H4	general transcription factor IIH subunit 4	3
64928	MRPL14	mitochondrial ribosomal protein L14	3
51651	PTRH2	peptidyl-tRNA hydrolase 2	3
23583	SMUG1	single-strand-selective monofunctional uracil-DNA glycosylase 1	3
7295	TXN	thioredoxin	3
2017	CTTN	cortactin	3
8493	PPM1D	protein phosphatase, Mg2+/Mn2+ dependent 1D	3
10813	UTP14A	UTP14A small subunit processome component	3
84267	C9orf64	chromosome 9 open reading frame 64	3
55276	PGM2	phosphoglucomutase 2	3
54606	DDX56	DEAD-box helicase 56	3
130367	SGPP2	sphingosine-1-phosphate phosphatase 2	3
1317	SLC31A1	solute carrier family 31 member 1	3
11333	PDAP1	PDGFA associated protein 1	3
51020	HDDC2	HD domain containing 2	3
23512	SUZ12	SUZ12 polycomb repressive complex 2 subunit	3
9927	MFN2	mitofusin 2	3
84365	NIFK	nucleolar protein interacting with the FHA domain of MKI67	3
80742	PRR3	proline rich 3	3
10557	RPP38	ribonuclease P/MRP subunit p38	3
26589	MRPL46	mitochondrial ribosomal protein L46	3
51491	NOP16	NOP16 nucleolar protein	3
10899	JTB	jumping translocation breakpoint	3
51218	GLRX5	glutaredoxin 5	3
11331	PHB2	prohibitin 2	3
10195	ALG3	ALG3, alpha-1,3- mannosyltransferase	3
6503	SLA	Src-like-adaptor	3
65993	MRPS34	mitochondrial ribosomal protein S34	3
6364	CCL20	C-C motif chemokine ligand 20	3
7551	ZNF3	zinc finger protein 3	4
53405	CLIC5	chloride intracellular channel 5	4
130589	GALM	galactose mutarotase	4
8574	AKR7A2	aldo-keto reductase family 7 member A2	4
29062	WDR91	WD repeat domain 91	4
6051	RNPEP	arginyl aminopeptidase	4
688	KLF5	Kruppel like factor 5	4
10620	ARID3B	AT-rich interaction domain 3B	4
144195	SLC2A14	solute carrier family 2 member 14	4
10475	TRIM38	tripartite motif containing 38	4
90529	STPG1	sperm tail PG-rich repeat containing 1	4
6195	RPS6KA1	ribosomal protein S6 kinase A1	4
864	RUNX3	runt related transcription factor 3	4
10474	TADA3	transcriptional adaptor 3	4
90589	ZNF625	zinc finger protein 625	4
84941	HSH2D	hematopoietic SH2 domain containing	4
127943	FCRLB	Fc receptor like B	4
54894	RNF43	ring finger protein 43	4
64121	RRAGC	Ras related GTP binding C	4
347732	CATSPER3	cation channel sperm associated 3	4
54914	FOCAD	focadhesin	4
90488	TMEM263	transmembrane protein 263	4
339201	ASB16-AS1	ASB16 antisense RNA 1	4
4641	MYO1C	myosin IC	4
92014	SLC25A51	solute carrier family 25 member 51	4
5871	MAP4K2	mitogen-activated protein kinase kinase kinase kinase 2	4
27010	TPK1	thiamin pyrophosphokinase 1	4
2043	EPHA4	EPH receptor A4	4
4603	MYBL1	MYB proto-oncogene like 1	4
83988	NCALD	neurocalcin delta	4
79158	GNPTAB	N-acetylglucosamine-1-phosphate transferase alpha and beta subunits	4
57646	USP28	ubiquitin specific peptidase 28	4
23403	FBXO46	F-box protein 46	4
11059	WWP1	WW domain containing E3 ubiquitin protein ligase 1	4
7700	ZNF141	zinc finger protein 141	4
5311	PKD2	polycystin 2, transient receptor potential cation channel	4

79627	OGFRL1	opioid growth factor receptor like 1	4
286827	TRIM59	tripartite motif containing 59	4
10902	BRD8	bromodomain containing 8	4
26269	FBXO8	F-box protein 8	4
11153	FICD	FIC domain containing	4
9846	GAB2	GRB2 associated binding protein 2	4
57580	PREX1	phosphatidylinositol-3,4,5-trisphosphate dependent Rac exchange factor 1	4
3248	HPGD	hydroxyprostaglandin dehydrogenase 15-(NAD)	4
133308	SLC9B2	solute carrier family 9 member B2	4
55650	PIGV	phosphatidylinositol glycan anchor biosynthesis class V	4
168374	ZNF92	zinc finger protein 92	4
115426	UHRF2	ubiquitin like with PHD and ring finger domains 2	4
100133211	LOC100133211	related RAS viral (r-ras) oncogene homolog 2 pseudogene	4
2800	GOLGA1	golgin A1	4
22858	ICK	intestinal cell kinase	4
64005	MYO1G	myosin IG	4
54820	NDE1	nudE neurodevelopment protein 1	4
81602	CDADC1	cytidine and dCMP deaminase domain containing 1	4
920	CD4	CD4 molecule	4
27013	CNPPD1	cyclin Pas1/PHO80 domain containing 1	4
84440	RAB11FIP4	RAB11 family interacting protein 4	4
9368	SLC9A3R1	SLC9A3 regulator 1	4
4798	NFRKB	nuclear factor related to kappaB binding protein	4
154141	MBOAT1	membrane bound O-acyltransferase domain containing 1	4
5867	RAB4A	RAB4A, member RAS oncogene family	4
54941	RNF125	ring finger protein 125	4
100131827	ZNF717	zinc finger protein 717	4
9814	SFI1	SFI1 centrin binding protein	4
55758	RCOR3	REST corepressor 3	4
149840	C20orf196	chromosome 20 open reading frame 196	4
222068	TMED4	transmembrane p24 trafficking protein 4	4
84993	UBL7	ubiquitin like 7	4
57493	HEG1	heart development protein with EGF like domains 1	4
652	BMP4	bone morphogenetic protein 4	4
6448	SGSH	N-sulfoglucosamine sulfohydrolase	4
5635	PRPSAP1	phosphoribosyl pyrophosphate synthetase associated protein 1	4
340061	TMEM173	transmembrane protein 173	4
51164	DCTN4	dynactin subunit 4	4
83986	FAM234A	family with sequence similarity 234 member A	4
440515	ZNF506	zinc finger protein 506	4
2185	PTK2B	protein tyrosine kinase 2 beta	4
9159	PCSK7	proprotein convertase subtilisin/kexin type 7	4
148137	PROSER3	proline and serine rich 3	4
84196	USP48	ubiquitin specific peptidase 48	4
2909	ARHGAP35	Rho GTPase activating protein 35	4
10194	TSHZ1	teashirt zinc finger homeobox 1	4
6482	ST3GAL1	ST3 beta-galactoside alpha-2,3-sialyltransferase 1	4
165918	RNF168	ring finger protein 168	4
1027	CDKN1B	cyclin dependent kinase inhibitor 1B	4
162962	ZNF836	zinc finger protein 836	4
90233	ZNF551	zinc finger protein 551	4
58986	TMEM8A	transmembrane protein 8A	4
80017	C14orf159	chromosome 14 open reading frame 159	4
8707	B3GALT2	beta-1,3-galactosyltransferase 2	4
8717	TRADD	TNFRSF1A associated via death domain	4
6293	VPS52	VPS52, GARP complex subunit	4
54843	SYTL2	synaptotagmin like 2	4
4126	MANBA	mannosidase beta	4
57589	RIC1	RIC1 homolog, RAB6A GEF complex partner 1	4
23233	EXOC6B	exocyst complex component 6B	4
22898	DENND3	DENN domain containing 3	4
157638	FAM84B	family with sequence similarity 84 member B	4
4644	MYO5A	myosin VA	4
51684	SUFU	SUFU negative regulator of hedgehog signaling	4
3956	LGALS1	galectin 1	4

79695	GALNT12	polypeptide N-acetylgalactosaminyltransferase 12	4
340252	ZNF680	zinc finger protein 680	4
8831	SYNGAP1	synaptic Ras GTPase activating protein 1	4
23625	FAM89B	family with sequence similarity 89 member B	4
92979	MARCH9	membrane associated ring-CH-type finger 9	4
9926	LPGAT1	lysophosphatidylglycerol acyltransferase 1	4
23218	NBEAL2	neurobeachin like 2	4
9975	NR1D2	nuclear receptor subfamily 1 group D member 2	4
11278	KLF12	Kruppel like factor 12	4
11184	MAP4K1	mitogen-activated protein kinase kinase kinase kinase 1	4
9467	SH3BP5	SH3 domain binding protein 5	4
4084	MXD1	MAX dimerization protein 1	4
23370	ARHGEF18	Rho/Rac guanine nucleotide exchange factor 18	4
5295	PIK3R1	phosphoinositide-3-kinase regulatory subunit 1	4
90139	TSPAN18	tetraspanin 18	4
11238	CA5B	carbonic anhydrase 5B	4
440068	CARD17	caspase recruitment domain family member 17	4
994	CDC25B	cell division cycle 25B	4
114804	RNF157	ring finger protein 157	4
84687	PPP1R9B	protein phosphatase 1 regulatory subunit 9B	4
5732	PTGER2	prostaglandin E receptor 2	4
6693	SPN	sialophorin	4
137835	TMEM71	transmembrane protein 71	4
818	CAMK2G	calcium/calmodulin dependent protein kinase II gamma	4
2081	ERN1	endoplasmic reticulum to nucleus signaling 1	4
373156	GSTK1	glutathione S-transferase kappa 1	4
9938	ARHGAP25	Rho GTPase activating protein 25	4
340547	VSIG1	V-set and immunoglobulin domain containing 1	4
6920	TCEA3	transcription elongation factor A3	4
8635	RNASET2	ribonuclease T2	4
114932	MRFAP1L1	Morf4 family associated protein 1 like 1	4
4615	MYD88	myeloid differentiation primary response 88	4
5443	POMC	proopiomelanocortin	4
10636	RGS14	regulator of G-protein signaling 14	4
6536	SLC6A9	solute carrier family 6 member 9	4
10125	RASGRP1	RAS guanyl releasing protein 1	4
441108	C5orf56	chromosome 5 open reading frame 56	4
51317	PHF21A	PHD finger protein 21A	4
11214	AKAP13	A-kinase anchoring protein 13	4
2035	EPB41	erythrocyte membrane protein band 4.1	4
10404	CPQ	carboxypeptidase Q	4
203328	SUSD3	sushi domain containing 3	4
4542	MYO1F	myosin IF	4
3587	IL10RA	interleukin 10 receptor subunit alpha	4
80321	CEP70	centrosomal protein 70	4
51135	IRAK4	interleukin 1 receptor associated kinase 4	4
54704	PDP1	pyruvate dehyrogenase phosphatase catalytic subunit 1	4
7096	TLR1	toll like receptor 1	4
57140	RNPEPL1	arginyl aminopeptidase like 1	4
79792	GSDMD	gasdermin D	4
2550	GABBR1	gamma-aminobutyric acid type B receptor subunit 1	4
8519	IFITM1	interferon induced transmembrane protein 1	4
3631	INPP4A	inositol polyphosphate-4-phosphatase type I A	4
22900	CARD8	caspase recruitment domain family member 8	4
7799	PRDM2	PR/SET domain 2	4
79865	TREML2	triggering receptor expressed on myeloid cells like 2	4
6311	ATXN2	ataxin 2	4
338799	LINC01089	long intergenic non-protein coding RNA 1089	4
1901	S1PR1	sphingosine-1-phosphate receptor 1	4
4194	MDM4	MDM4, p53 regulator	4
8737	RIPK1	receptor interacting serine/threonine kinase 1	4
51185	CRBN	cereblon	4
64108	RTP4	receptor transporter protein 4	4
23351	KHNYN	KH and NYN domain containing	4
5899	RALB	RAS like proto-oncogene B	4

100506334	LINC00649	long intergenic non-protein coding RNA 649	4
128338	DRAM2	DNA damage regulated autophagy modulator 2	4
283349	RASSF3	Ras association domain family member 3	4
222255	ATXN7L1	ataxin 7 like 1	4
409	ARRB2	arrestin beta 2	4
9674	KIAA0040	KIAA0040	4
7360	UGP2	UDP-glucose pyrophosphorylase 2	4
51246	SHISA5	shisa family member 5	4
9985	REC8	REC8 meiotic recombination protein	4
283130	SLC25A45	solute carrier family 25 member 45	4
59339	PLEKHA2	pleckstrin homology domain containing A2	4
10577	NPC2	NPC intracellular cholesterol transporter 2	4
3120	HLA-DQB2	major histocompatibility complex, class II, DQ beta 2	4
54870	QRICH1	glutamine rich 1	4
78991	PCYOX1L	prenylcysteine oxidase 1 like	4
64863	METTL4	methyltransferase like 4	4
4240	MFGE8	milk fat globule-EGF factor 8 protein	4
51439	FAM8A1	family with sequence similarity 8 member A1	4
10140	TOB1	transducer of ERBB2, 1	4
23484	LEPROTL1	leptin receptor overlapping transcript-like 1	4
51292	GMPR2	guanosine monophosphate reductase 2	4
120224	TMEM45B	transmembrane protein 45B	4
9337	CNOT8	CCR4-NOT transcription complex subunit 8	4
23582	CCNDBP1	cyclin D1 binding protein 1	4
284309	ZNF776	zinc finger protein 776	4
8440	NCK2	NCK adaptor protein 2	4
10581	IFITM2	interferon induced transmembrane protein 2	4
51390	AIG1	androgen induced 1	4
56477	CCL28	C-C motif chemokine ligand 28	4
201627	DENND6A	DENN domain containing 6A	4
101	ADAM8	ADAM metallopeptidase domain 8	4
10311	DSCR3	DSCR3 arrestin fold containing	4
156	GRK2	G protein-coupled receptor kinase 2	4
55339	WDR33	WD repeat domain 33	4
90736	FAM104B	family with sequence similarity 104 member B	4
64857	PLEKHG2	pleckstrin homology and RhoGEF domain containing G2	4
54813	KLHL28	kelch like family member 28	4
140461	ASB8	ankyrin repeat and SOCS box containing 8	4
81846	SBF2	SET binding factor 2	4
25943	C20orf194	chromosome 20 open reading frame 194	4
54868	TMEM104	transmembrane protein 104	4
23171	GPD1L	glycerol-3-phosphate dehydrogenase 1-like	4
2745	GLRX	glutaredoxin	4
54970	TTC12	tetratricopeptide repeat domain 12	4
84614	ZBTB37	zinc finger and BTB domain containing 37	4
828	CAPS	calcyphosine	4
1659	DHX8	DEAH-box helicase 8	4
147694	ZNF548	zinc finger protein 548	4
26036	ZNF451	zinc finger protein 451	4
285550	FAM200B	family with sequence similarity 200 member B	4
147658	ZNF534	zinc finger protein 534	4
147923	ZNF420	zinc finger protein 420	4
7536	SF1	splicing factor 1	4
285596	FAM153A	family with sequence similarity 153 member A	4
57452	GALNT16	polypeptide N-acetylgalactosaminyltransferase 16	4
56339	METTL3	methyltransferase like 3	4
100129842	ZNF737	zinc finger protein 737	4
124460	SNX20	sorting nexin 20	4
51696	HECA	hdc homolog, cell cycle regulator	4
6811	STX5	syntaxin 5	4
51643	TMBIM4	transmembrane BAX inhibitor motif containing 4	4
388650	FAM69A	family with sequence similarity 69 member A	4
8027	STAM	signal transducing adaptor molecule	4
4850	CNOT4	CCR4-NOT transcription complex subunit 4	4
4676	NAP1L4	nucleosome assembly protein 1 like 4	4

7690	ZNF131	zinc finger protein 131	4
6789	STK4	serine/threonine kinase 4	4
55634	KRBOX4	KRAB box domain containing 4	4
63897	HEATR6	HEAT repeat containing 6	4
1374	CPT1A	carnitine palmitoyltransferase 1A	4
6402	SELL	selectin L	4
7592	ZNF41	zinc finger protein 41	4
372	ARCN1	archain 1	4
23451	SF3B1	splicing factor 3b subunit 1	4
163081	ZNF567	zinc finger protein 567	4
7381	UQCRB	ubiquinol-cytochrome c reductase binding protein	4
6230	RPS25	ribosomal protein S25	4
83452	RAB33B	RAB33B, member RAS oncogene family	4
56987	BBX	BBX, HMG-box containing	4
9541	CIR1	corepressor interacting with RBPJ, 1	4
9534	ZNF254	zinc finger protein 254	4
54986	ULK4	unc-51 like kinase 4	4
64421	DCLRE1C	DNA cross-link repair 1C	4
51531	TRMO	tRNA methyltransferase O	4
114781	BTBD9	BTB domain containing 9	4
5150	PDE7A	phosphodiesterase 7A	4
55729	ATF7IP	activating transcription factor 7 interacting protein	4
285343	TCAIM	T-cell activation inhibitor, mitochondrial	4
6671	SP4	Sp4 transcription factor	4
9252	RPS6KA5	ribosomal protein S6 kinase A5	4
64940	STAG3L4	stromal antigen 3-like 4 (pseudogene)	4
10681	GNB5	G protein subunit beta 5	4
3845	KRAS	KRAS proto-oncogene, GTPase	4
54542	RC3H2	ring finger and CCCH-type domains 2	4
961	CD47	CD47 molecule	4
84084	RAB6C	RAB6C, member RAS oncogene family	4
22883	CLSTN1	calsyntenin 1	4
3385	ICAM3	intercellular adhesion molecule 3	4
57533	TBC1D14	TBC1 domain family member 14	4
375743	PTAR1	protein prenyltransferase alpha subunit repeat containing 1	4
3738	KCNA3	potassium voltage-gated channel subfamily A member 3	4
9697	TRAM2	translocation associated membrane protein 2	4
55296	TBC1D19	TBC1 domain family member 19	4
9873	FCHSD2	FCH and double SH3 domains 2	4
105371242	LOC105371242	peptidyl-prolyl cis-trans isomerase A-like 4C	4
643836	ZFP62	ZFP62 zinc finger protein	4
23161	SNX13	sorting nexin 13	4
9197	SLC33A1	solute carrier family 33 member 1	4
1955	MEGF9	multiple EGF like domains 9	4
57198	ATP8B2	ATPase phospholipid transporting 8B2	4
105372141	LOC105372141	uncharacterized LOC105372141	4
9798	IST1	IST1, ESCRT-III associated factor	4
54521	WDR44	WD repeat domain 44	4
57534	MIB1	mindbomb E3 ubiquitin protein ligase 1	4
84124	ZNF394	zinc finger protein 394	4
25852	ARMC8	armadillo repeat containing 8	4
54739	XAF1	XIAP associated factor 1	4
8869	ST3GAL5	ST3 beta-galactoside alpha-2,3-sialyltransferase 5	4
5027	P2RX7	purinergic receptor P2X 7	4
51	ACOX1	acyl-CoA oxidase 1	4
9482	STX8	syntaxin 8	4
84079	ANKRD27	ankyrin repeat domain 27	4
10855	HPSE	heparanase	4
23097	CDK19	cyclin dependent kinase 19	4
54149	C21orf91	chromosome 21 open reading frame 91	4
9258	MFHAS1	malignant fibrous histiocytoma amplified sequence 1	4
5613	PRKX	protein kinase, X-linked	4
8237	USP11	ubiquitin specific peptidase 11	4
134553	C5orf24	chromosome 5 open reading frame 24	4
9913	SUPT7L	SPT7-like STAGA complex gamma subunit	4

64077	LHPP	phospholysine phosphohistidine inorganic pyrophosphate phosphatase	4
28232	SLCO3A1	solute carrier organic anion transporter family member 3A1	4
51606	ATP6V1H	ATPase H+ transporting V1 subunit H	4
83541	FAM110A	family with sequence similarity 110 member A	4
146857	SLFN13	schlafen family member 13	4
136895	C7orf31	chromosome 7 open reading frame 31	4
360023	ZBTB41	zinc finger and BTB domain containing 41	4
56985	ADPRM	ADP-ribose/CDP-alcohol diphosphatase, manganese dependent	4
92799	SHKBP1	SH3KBP1 binding protein 1	4
23199	GSE1	Gse1 coiled-coil protein	4
259197	NCR3	natural cytotoxicity triggering receptor 3	4
10299	MARCH6	membrane associated ring-CH-type finger 6	4
1757	SARDH	sarcosine dehydrogenase	4
27005	USP21	ubiquitin specific peptidase 21	4
51244	CCDC174	coiled-coil domain containing 174	4
8573	CASK	calcium/calmodulin dependent serine protein kinase	4
8603	FAM193A	family with sequence similarity 193 member A	4
26043	UBXN7	UBX domain protein 7	4
57105	CYSLTR2	cysteinyl leukotriene receptor 2	4
55180	LINS1	lines homolog 1	4
153642	ARSK	arylsulfatase family member K	4
91663	MYADM	myeloid associated differentiation marker	4
23131	GPATCH8	G-patch domain containing 8	4
11143	KAT7	lysine acetyltransferase 7	4
23259	DDHD2	DDHD domain containing 2	4
148268	ZNF570	zinc finger protein 570	4
50809	HP1BP3	heterochromatin protein 1 binding protein 3	4
9991	PTBP3	polypyrimidine tract binding protein 3	4
285513	GPRIN3	GPRIN family member 3	4
1859	DYRK1A	dual specificity tyrosine phosphorylation regulated kinase 1A	4
10513	APPBP2	amyloid beta precursor protein binding protein 2	4
27252	KLHL20	kelch like family member 20	4
374354	NHLRC2	NHL repeat containing 2	4
7159	TP53BP2	tumor protein p53 binding protein 2	4
27018	BEX3	brain expressed X-linked 3	4
7433	VIPR1	vasoactive intestinal peptide receptor 1	4
9946	CRYZL1	crystallin zeta like 1	4
23229	ARHGEF9	Cdc42 guanine nucleotide exchange factor 9	4
286336	FAM78A	family with sequence similarity 78 member A	4
6809	STX3	syntaxin 3	4
8776	MTMR1	myotubularin related protein 1	4
8545	CGGBP1	CGG triplet repeat binding protein 1	4
26136	TES	testin LIM domain protein	4
93594	TBC1D31	TBC1 domain family member 31	4
51281	ANKMY1	ankyrin repeat and MYND domain containing 1	4
58486	ZBED5	zinc finger BED-type containing 5	4
4253	MIA2	melanoma inhibitory activity 2	4
4170	MCL1	BCL2 family apoptosis regulator	4
2272	FHIT	fragile histidine triad	4
10866	HCP5	HLA complex P5 (non-protein coding)	4
57396	CLK4	CDC like kinase 4	4
171425	CLYBL	citrate lyase beta like	4
7248	TSC1	tuberous sclerosis 1	4
129685	TAF8	TATA-box binding protein associated factor 8	4
22920	KIFAP3	kinesin associated protein 3	4
159091	FAM122C	family with sequence similarity 122C	4
25957	PNISR	PNN interacting serine and arginine rich protein	4
91300	R3HDM4	R3H domain containing 4	4
51427	ZNF107	zinc finger protein 107	4
168850	ZNF800	zinc finger protein 800	4
2273	FHL1	four and a half LIM domains 1	4
10392	NOD1	nucleotide binding oligomerization domain containing 1	4
1656	DDX6	DEAD-box helicase 6	4
3991	LIPE	lipase E, hormone sensitive type	4
91949	COG7	component of oligomeric golgi complex 7	4

57120	GOPC	golgi associated PDZ and coiled-coil motif containing	4
84911	ZNF382	zinc finger protein 382	4
125488	TTC39C	tetratricopeptide repeat domain 39C	4
51752	ERAP1	endoplasmic reticulum aminopeptidase 1	4
222236	NAPEPLD	N-acyl phosphatidylethanolamine phospholipase D	4
54331	GNG2	G protein subunit gamma 2	4
23248	RPRD2	regulation of nuclear pre-mRNA domain containing 2	4
4940	OAS3	2'-5'-oligoadenylate synthetase 3	4
2011	MARK2	microtubule affinity regulating kinase 2	4
56882	CDC42SE1	CDC42 small effector 1	4
23635	SSBP2	single stranded DNA binding protein 2	4
4149	MAX	MYC associated factor X	4
51199	NIN	ninein	4
285195	SLC9A9	solute carrier family 9 member A9	4
8473	OGT	O-linked N-acetylglucosamine (GlcNAc) transferase	4
285440	CYP4V2	cytochrome P450 family 4 subfamily V member 2	4
9709	HERPUD1	homocysteine inducible ER protein with ubiquitin like domain 1	4
54816	ZNF280D	zinc finger protein 280D	4
26578	OSTF1	osteoclast stimulating factor 1	4
6815	STYX	serine/threonine/tyrosine interacting protein	4
663	BNIP2	BCL2 interacting protein 2	4
9779	TBC1D5	TBC1 domain family member 5	4
55773	TBC1D23	TBC1 domain family member 23	4
57185	NIPAL3	NIPA like domain containing 3	4
23204	ARL6IP1	ADP ribosylation factor like GTPase 6 interacting protein 1	4
8773	SNAP23	synaptosome associated protein 23	4
6303	SAT1	spermidine/spermine N1-acetyltransferase 1	4
57560	IFT80	intraflagellar transport 80	4
2948	GSTM4	glutathione S-transferase mu 4	4
3115	HLA-DPB1	major histocompatibility complex, class II, DP beta 1	4
79668	PARP8	poly(ADP-ribose) polymerase family member 8	4
4707	NDUFB1	NADH:ubiquinone oxidoreductase subunit B1	4
22901	ARSG	arylsulfatase G	4
84343	HPS3	HPS3, biogenesis of lysosomal organelles complex 2 subunit 1	4
54407	SLC38A2	solute carrier family 38 member 2	4
50999	TMED5	transmembrane p24 trafficking protein 5	4
3958	LGALS3	galectin 3	4
64840	PORCN	porcupine homolog (Drosophila)	4
5562	PRKAA1	protein kinase AMP-activated catalytic subunit alpha 1	4
9039	UBA3	ubiquitin like modifier activating enzyme 3	4
57649	PHF12	PHD finger protein 12	4
90806	ANGEL2	angel homolog 2	4
7581	ZNF33A	zinc finger protein 33A	4
375248	ANKRD36	ankyrin repeat domain 36	4
8821	INPP4B	inositol polyphosphate-4-phosphatase type II B	4
23613	ZMYND8	zinc finger MYND-type containing 8	4
567	B2M	beta-2-microglobulin	4
9666	DZIP3	DAZ interacting zinc finger protein 3	4
3459	IFNGR1	interferon gamma receptor 1	4
55285	RBM41	RNA binding motif protein 41	4
201895	SMIM14	small integral membrane protein 14	4
29058	TMEM230	transmembrane protein 230	4
9958	USP15	ubiquitin specific peptidase 15	4
917	CD3G	CD3g molecule	4
10181	RBM5	RNA binding motif protein 5	4
55788	LMBRD1	LMBR1 domain containing 1	4
6814	STXBP3	syntaxin binding protein 3	4
1666	DECR1	2,4-dienoyl-CoA reductase 1, mitochondrial	4
51506	UFC1	ubiquitin-fold modifier conjugating enzyme 1	4
6281	S100A10	S100 calcium binding protein A10	4
28962	OSTM1	osteopetrosis associated transmembrane protein 1	4
54677	CROT	carnitine O-octanoyltransferase	4
8799	PEX11B	peroxisomal biogenesis factor 11 beta	4
1730	DIAPH2	diaphanous related formin 2	4
9694	EMC2	ER membrane protein complex subunit 2	4

7181	NR2C1	nuclear receptor subfamily 2 group C member 1	4
51108	METTL9	methyltransferase like 9	4
27141	CIDEB	cell death-inducing DFFA-like effector b	4
64376	IKZF5	IKAROS family zinc finger 5	4
7756	ZNF207	zinc finger protein 207	4
256471	MFSD8	major facilitator superfamily domain containing 8	4
3660	IRF2	interferon regulatory factor 2	4
64431	ACTR6	ARP6 actin-related protein 6 homolog	4
79872	CBLL1	Cbl proto-oncogene like 1	4
337976	KRTAP20-2	keratin associated protein 20-2	4
51347	TAOK3	TAO kinase 3	4
1998	ELF2	E74 like ETS transcription factor 2	4
84236	RHBDD1	rhomboid domain containing 1	4
89978	DPH6	diphthamine biosynthesis 6	4
8767	RIPK2	receptor interacting serine/threonine kinase 2	4
79096	C11orf49	chromosome 11 open reading frame 49	4
5930	RBBP6	RB binding protein 6, ubiquitin ligase	4
645142	PPIAL4D	peptidylprolyl isomerase A like 4D	4
148867	SLC30A7	solute carrier family 30 member 7	4
145389	SLC38A6	solute carrier family 38 member 6	4
26115	TANC2	tetratricopeptide repeat, ankyrin repeat and coiled-coil containing 2	4
26515	TIMM10B	translocase of inner mitochondrial membrane 10 homolog B (yeast)	4
10491	CRTAP	cartilage associated protein	4
962	CD48	CD48 molecule	4
3128	HLA-DRB6	major histocompatibility complex, class II, DR beta 6 (pseudogene)	4
84333	PCGF5	polycomb group ring finger 5	4
6301	SARS	seryl-tRNA synthetase	4
148362	BROX	BRO1 domain and CAAX motif containing	4
51322	WAC	WW domain containing adaptor with coiled-coil	4
2060	EPS15	epidermal growth factor receptor pathway substrate 15	4
64747	MFSD1	major facilitator superfamily domain containing 1	4
79745	CLIP4	CAP-Gly domain containing linker protein family member 4	4
84272	YIPF4	Yip1 domain family member 4	4
3163	HMOX2	heme oxygenase 2	4
1521	CTSW	cathepsin W	4
85025	TMEM60	transmembrane protein 60	4
56674	TMEM9B	TMEM9 domain family member B	4
3384	ICAM2	intercellular adhesion molecule 2	4
26061	HACL1	2-hydroxyacyl-CoA lyase 1	4
27065	NSG1	neuron specific gene family member 1	4
29994	BAZ2B	bromodomain adjacent to zinc finger domain 2B	4
6643	SNX2	sorting nexin 2	4
27240	SIT1	signaling threshold regulating transmembrane adaptor 1	4
3117	HLA-DQA1	major histocompatibility complex, class II, DQ alpha 1	4
27163	NAAA	N-acylethanolamine acid amidase	4
84795	PYROXD2	pyridine nucleotide-disulphide oxidoreductase domain 2	4
8667	EIF3H	eukaryotic translation initiation factor 3 subunit H	4
254887	ZDHHC23	zinc finger DHHC-type containing 23	4
124961	ZFP3	ZFP3 zinc finger protein	4
26071	FAM127B	family with sequence similarity 127 member B	4
23149	FCHO1	FCH domain only 1	4
374395	TMEM179B	transmembrane protein 179B	4
3688	ITGB1	integrin subunit beta 1	4
4711	NDUFB5	NADH:ubiquinone oxidoreductase subunit B5	4
9871	SEC24D	SEC24 homolog D, COPII coat complex component	4
56898	BDH2	3-hydroxybutyrate dehydrogenase, type 2	4
23585	TMEM50A	transmembrane protein 50A	4
3133	HLA-E	major histocompatibility complex, class I, E	4
124512	METTL23	methyltransferase like 23	4
11000	SLC27A3	solute carrier family 27 member 3	4
126626	GABPB2	GA binding protein transcription factor beta subunit 2	4
257160	RNF214	ring finger protein 214	4
9649	RALGPS1	Ral GEF with PH domain and SH3 binding motif 1	4
26273	FBXO3	F-box protein 3	4
54509	RHOF	ras homolog family member F, filopodia associated	4

285093	RTP5	receptor transporter protein 5 (putative)	4
25793	FBXO7	F-box protein 7	4
7770	ZNF227	zinc finger protein 227	4
85403	EAF1	ELL associated factor 1	4
4582	MUC1	mucin 1, cell surface associated	4
1029	CDKN2A	cyclin dependent kinase inhibitor 2A	4
3717	JAK2	Janus kinase 2	4
1992	SERPINB1	serpin family B member 1	4
25821	MTO1	mitochondrial tRNA translation optimization 1	4
51635	DHRS7	dehydrogenase/reductase 7	4
51747	LUC7L3	LUC7 like 3 pre-mRNA splicing factor	4
10628	TXNIP	thioredoxin interacting protein	4
5533	PPP3CC	protein phosphatase 3 catalytic subunit gamma	4
5130	PCYT1A	phosphate cytidylyltransferase 1, choline, alpha	4
10219	KLRG1	killer cell lectin like receptor G1	4
3127	HLA-DRB5	major histocompatibility complex, class II, DR beta 5	4
253461	ZBTB38	zinc finger and BTB domain containing 38	4
80267	EDEM3	ER degradation enhancing alpha-mannosidase like protein 3	4
149628	PYHIN1	pyrin and HIN domain family member 1	4
55508	SLC35E3	solute carrier family 35 member E3	4
89853	MVB12B	multivesicular body subunit 12B	4
2313	FLI1	Fli-1 proto-oncogene, ETS transcription factor	4
79591	C10orf76	chromosome 10 open reading frame 76	4
9204	ZMYM6	zinc finger MYM-type containing 6	4
25975	EGFL6	EGF like domain multiple 6	4
10039	PARP3	poly(ADP-ribose) polymerase family member 3	4
54855	FAM46C	family with sequence similarity 46 member C	4
171586	ABHD3	abhydrolase domain containing 3	4
55809	TRERF1	transcriptional regulating factor 1	4
115825	WDFY2	WD repeat and FYVE domain containing 2	4
23059	CLUAP1	clusterin associated protein 1	4
79877	DCAKD	dephospho-CoA kinase domain containing	4
84273	NOA1	nitric oxide associated 1	4
4835	NQO2	NAD(P)H quinone dehydrogenase 2	4
283237	TTC9C	tetratricopeptide repeat domain 9C	4
5797	PTPRM	protein tyrosine phosphatase, receptor type M	4
3820	KLRB1	killer cell lectin like receptor B1	4
4217	MAP3K5	mitogen-activated protein kinase kinase kinase 5	4
64773	PCED1A	PC-esterase domain containing 1A	4
2054	STX2	syntaxin 2	4
824	CAPN2	calpain 2	4
79577	CDC73	cell division cycle 73	4
3108	HLA-DMA	major histocompatibility complex, class II, DM alpha	4
154075	SAMD3	sterile alpha motif domain containing 3	4
7905	REEP5	receptor accessory protein 5	4
199704	ZNF585A	zinc finger protein 585A	4
88455	ANKRD13A	ankyrin repeat domain 13A	4
6668	SP2	Sp2 transcription factor	4
1604	CD55	CD55 molecule (Cromer blood group)	4
64420	SUSD1	sushi domain containing 1	4
1235	CCR6	C-C motif chemokine receptor 6	4
2838	GPR15	G protein-coupled receptor 15	4
440026	TMEM41B	transmembrane protein 41B	4
729230	CCR2	C-C motif chemokine receptor 2	4
94101	ORMDL1	ORMDL sphingolipid biosynthesis regulator 1	4
1075	CTSC	cathepsin C	4
90624	LYRM7	LYR motif containing 7	4
801	CALM1	calmodulin 1	4
55967	NDUFA12	NADH:ubiquinone oxidoreductase subunit A12	4
8477	GPR65	G protein-coupled receptor 65	4
57544	TXNDC16	thioredoxin domain containing 16	4
1512	CTSH	cathepsin H	4
84902	CEP89	centrosomal protein 89	4
7576	ZNF28	zinc finger protein 28	4
29116	MYLIP	myosin regulatory light chain interacting protein	4

50808	AK3	adenylate kinase 3	4
7289	TULP3	tubby like protein 3	4
6166	RPL36AL	ribosomal protein L36a like	4
54414	SIAE	sialic acid acetylesterase	4
23673	STX12	syntaxin 12	4
833	CARS	cysteinyl-tRNA synthetase	4
7940	LST1	leukocyte specific transcript 1	4
2040	STOM	stomatin	4
5720	PSME1	proteasome activator subunit 1	4
51101	ZC2HC1A	zinc finger C2HC-type containing 1A	4
1102	RCBTB2	RCC1 and BTB domain containing protein 2	4
2752	GLUL	glutamate-ammonia ligase	4
3123	HLA-DRB1	major histocompatibility complex, class II, DR beta 1	4
23608	MKRN1	makorin ring finger protein 1	4
5429	POLH	DNA polymerase eta	4
100507463	PSMB8-AS1	PSMB8 antisense RNA 1 (head to head)	4
4261	CIITA	class II major histocompatibility complex transactivator	4
6916	TBXAS1	thromboxane A synthase 1	4
116496	FAM129A	family with sequence similarity 129 member A	4
643911	CRNDE	colorectal neoplasia differentially expressed (non-protein coding)	4
4094	MAF	MAF bZIP transcription factor	4
10788	IQGAP2	IQ motif containing GTPase activating protein 2	4
3122	HLA-DRA	major histocompatibility complex, class II, DR alpha	4
3113	HLA-DPA1	major histocompatibility complex, class II, DP alpha 1	4
196527	ANO6	anoctamin 6	4
10370	CITED2	Cbp/p300 interacting transactivator with Glu/Asp rich carboxy-terminal domain 2	4
941	CD80	CD80 molecule	4
202	AIM1	absent in melanoma 1	4
2664	GDI1	GDP dissociation inhibitor 1	4
6609	SMPD1	sphingomyelin phosphodiesterase 1	4
84138	SLC7A6OS	solute carrier family 7 member 6 opposite strand	4
254251	LCORL	ligand dependent nuclear receptor corepressor like	4
2643	GCH1	GTP cyclohydrolase 1	4
1633	DCK	deoxycytidine kinase	4
64127	NOD2	nucleotide binding oligomerization domain containing 2	4
51061	TXNDC11	thioredoxin domain containing 11	4
5451	POU2F1	POU class 2 homeobox 1	4
29968	PSAT1	phosphoserine aminotransferase 1	4
4939	OAS2	2'-5'-oligoadenylate synthetase 2	4
669	BPGM	bisphosphoglycerate mutase	4
5165	PDK3	pyruvate dehydrogenase kinase 3	4
79823	CAMKMT	calmodulin-lysine N-methyltransferase	4
1979	EIF4EBP2	eukaryotic translation initiation factor 4E binding protein 2	4
54495	TMX3	thioredoxin related transmembrane protein 3	4
80350	LPAL2	lipoprotein(a) like 2, pseudogene	4
51703	ACSL5	acyl-CoA synthetase long-chain family member 5	4
4267	CD99	CD99 molecule	4
152007	GLIPR2	GLI pathogenesis related 2	4
79071	ELOVL6	ELOVL fatty acid elongase 6	4
26277	TINF2	TERF1 interacting nuclear factor 2	4
388323	GLTPD2	glycolipid transfer protein domain containing 2	5
348262	MCRIP1	MAPK regulated corepressor interacting protein 1	5
770	CA11	carbonic anhydrase 11	5
140606	SELENOM	selenoprotein M	5
7643	ZNF90	zinc finger protein 90	5
5118	PCOLCE	procollagen C-endopeptidase enhancer	5
27113	BBC3	BCL2 binding component 3	5
60	ACTB	actin beta	5
4137	MAPT	microtubule associated protein tau	5
2051	EPHB6	EPH receptor B6	5
9435	CHST2	carbohydrate sulfotransferase 2	5
810	CALML3	calmodulin like 3	5
84513	PLPP5	phospholipid phosphatase 5	5
1406	CRX	cone-rod homeobox	5
23178	PASK	PAS domain containing serine/threonine kinase	5

84310	C7orf50	chromosome 7 open reading frame 50	5
56125	PCDHB11	protocadherin beta 11	5
440073	IQSEC3	IQ motif and Sec7 domain 3	5
2889	RAPGEF1	Rap guanine nucleotide exchange factor 1	5
865	CBFB	core-binding factor beta subunit	5
157	GRK3	G protein-coupled receptor kinase 3	5
100462981	MTRNR2L2	MT-RNR2-like 2	5
51764	GNG13	G protein subunit gamma 13	5
353134	LCE1D	late cornified envelope 1D	5
64743	WDR13	WD repeat domain 13	5
80194	TMEM134	transmembrane protein 134	5
23678	SGK3	serum/glucocorticoid regulated kinase family member 3	5
115703	ARHGAP33	Rho GTPase activating protein 33	5
100316904	SAP25	Sin3A associated protein 25	5
256949	KANK3	KN motif and ankyrin repeat domains 3	5
9990	SLC12A6	solute carrier family 12 member 6	5
83593	RASSF5	Ras association domain family member 5	5
126695	KDF1	keratinocyte differentiation factor 1	5
100130958	SYCE1L	synaptonemal complex central element protein 1 like	5
286075	ZNF707	zinc finger protein 707	5
85407	NKD1	naked cuticle homolog 1	5
753	LDLRAD4	low density lipoprotein receptor class A domain containing 4	5
23417	MLYCD	malonyl-CoA decarboxylase	5
284723	SLC25A34	solute carrier family 25 member 34	5
348013	TMEM255B	transmembrane protein 255B	5
85027	SMIM3	small integral membrane protein 3	5
388595	TMEM82	transmembrane protein 82	5
535	ATP6V0A1	ATPase H+ transporting V0 subunit a1	5
9531	BAG3	BCL2 associated athanogene 3	5
915	CD3D	CD3d molecule	5
10507	SEMA4D	semaphorin 4D	5
56940	DUSP22	dual specificity phosphatase 22	5
55030	FBXO34	F-box protein 34	5
10765	KDM5B	lysine demethylase 5B	5
921	CD5	CD5 molecule	5
6223	RPS19	ribosomal protein S19	5
132299	OCIAD2	OCIA domain containing 2	5
341567	H1FNT	H1 histone family member N, testis specific	5
64061	TSPYL2	TSPY like 2	5
27086	FOXP1	forkhead box P1	5
6821	SUOX	sulfite oxidase	5
57092	PCNP	PEST proteolytic signal containing nuclear protein	5
93145	OLFM2	olfactomedin 2	5
129804	FBLN7	fibulin 7	5
79778	MICALL2	MICAL like 2	5
1514	CTSL	cathepsin L	5
1543	CYP1A1	cytochrome P450 family 1 subfamily A member 1	5
23275	POFUT2	protein O-fucosyltransferase 2	5
148223	C19orf25	chromosome 19 open reading frame 25	5
268	AMH	anti-Mullerian hormone	5
10362	HMG20B	high mobility group 20B	5
116983	ACAP3	ArfGAP with coiled-coil, ankyrin repeat and PH domains 3	5
9792	SERTAD2	SERTA domain containing 2	5
9057	SLC7A6	solute carrier family 7 member 6	5
5209	PFKFB3	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3	5
84947	SERAC1	serine active site containing 1	5
10927	SPIN1	spindlin 1	5
100463487	MTRNR2L9	MT-RNR2-like 9	5
203522	INTS6L	integrator complex subunit 6 like	5
94235	GNG8	G protein subunit gamma 8	5
6001	RGS10	regulator of G-protein signaling 10	5
54947	LPCAT2	lysophosphatidylcholine acyltransferase 2	5
659	BMPR2	bone morphogenetic protein receptor type 2	5
23479	ISCU	iron-sulfur cluster assembly enzyme	5
100287898	TTC34	tetratricopeptide repeat domain 34	5

2908	NR3C1	nuclear receptor subfamily 3 group C member 1	5
6229	RPS24	ribosomal protein S24	5
29121	CLEC2D	C-type lectin domain family 2 member D	5
25893	TRIM58	tripartite motif containing 58	5
29095	ORMDL2	ORMDL sphingolipid biosynthesis regulator 2	5
104	ADARB1	adenosine deaminase, RNA specific B1	5
5272	SERPINB9	serpin family B member 9	5
284611	FAM102B	family with sequence similarity 102 member B	5
27248	ERLEC1	endoplasmic reticulum lectin 1	5
10982	MAPRE2	microtubule associated protein RP/EB family member 2	5
6794	STK11	serine/threonine kinase 11	5
3831	KLC1	kinesin light chain 1	5
6242	RTKN	rhotekin	5
57680	CHD8	chromodomain helicase DNA binding protein 8	5
85364	ZCCHC3	zinc finger CCHC-type containing 3	5
163126	EID2	EP300 interacting inhibitor of differentiation 2	5
650669	GAS6-AS1	GAS6 antisense RNA 1	5
55893	ZNF395	zinc finger protein 395	5
26228	STAP1	signal transducing adaptor family member 1	5
51225	ABI3	ABI family member 3	5
7187	TRAF3	TNF receptor associated factor 3	5
196	AHR	aryl hydrocarbon receptor	5
728747	ANKRD20A4	ankyrin repeat domain 20 family member A4	5
389333	PROB1	proline rich basic protein 1	5
11202	KLK8	kallikrein related peptidase 8	5
2530	FUT8	fucosyltransferase 8	5
6224	RPS20	ribosomal protein S20	5
55636	CHD7	chromodomain helicase DNA binding protein 7	5
10188	TNK2	tyrosine kinase non receptor 2	5
170067	SUPT20HL2	SPT20 homolog, SAGA complex component-like 2	5
4363	ABCC1	ATP binding cassette subfamily C member 1	5
581	BAX	BCL2 associated X, apoptosis regulator	5
7529	YWHAB	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein beta	5
60468	BACH2	BTB domain and CNC homolog 2	5
57491	AHRR	aryl-hydrocarbon receptor repressor	5
730098	LOC730098	uncharacterized LOC730098	5
221937	FOXK1	forkhead box K1	5
729020	RPEL1	ribulose-5-phosphate-3-epimerase like 1	5
4082	MARCKS	myristoylated alanine rich protein kinase C substrate	5
5290	PIK3CA	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha	5
63971	KIF13A	kinesin family member 13A	5
9794	MAML1	mastermind like transcriptional coactivator 1	5
80045	GPR157	G protein-coupled receptor 157	5
3097	HIVEP2	human immunodeficiency virus type I enhancer binding protein 2	5
7044	LEFTY2	left-right determination factor 2	5
222658	KCTD20	potassium channel tetramerization domain containing 20	5
399668	SMIM10L2A	small integral membrane protein 10 like 2A	5
125058	TBC1D16	TBC1 domain family member 16	5
5753	PTK6	protein tyrosine kinase 6	5
65986	ZBTB10	zinc finger and BTB domain containing 10	5
727957	MROH1	maestro heat like repeat family member 1	5
2779	GNAT1	G protein subunit alpha transducin 1	5
376497	SLC27A1	solute carrier family 27 member 1	5
1427	CRYGS	crystallin gamma S	5
440955	TMEM89	transmembrane protein 89	5
9883	POM121	POM121 transmembrane nucleoporin	5
54863	TOR4A	torsin family 4 member A	5
8878	SQSTM1	sequestosome 1	5
414318	C9orf106	chromosome 9 open reading frame 106	5
7146	TNXA	tenascin XA (pseudogene)	5
6498	SKIL	SKI like proto-oncogene	5
3090	HIC1	hypermethylated in cancer 1	5
22877	MLXIP	MLX interacting protein	5
3853	KRT6A	keratin 6A	5
84878	ZBTB45	zinc finger and BTB domain containing 45	5

359948	IRF2BP2	interferon regulatory factor 2 binding protein 2	5
23505	TMEM131	transmembrane protein 131	5
10489	LRRC41	leucine rich repeat containing 41	5
717	C2	complement C2	5
10014	HDAC5	histone deacetylase 5	5
3910	LAMA4	laminin subunit alpha 4	5
6623	SNCG	synuclein gamma	5
90427	BMF	Bcl2 modifying factor	5
6209	RPS15	ribosomal protein S15	5
6205	RPS11	ribosomal protein S11	5
6217	RPS16	ribosomal protein S16	5
158376	LINC00961	long intergenic non-protein coding RNA 961	5
79791	FBXO31	F-box protein 31	5
54795	TRPM4	transient receptor potential cation channel subfamily M member 4	5
7791	ZYX	zyxin	5
123920	CMTM3	CKLF like MARVEL transmembrane domain containing 3	5
3718	JAK3	Janus kinase 3	5
11336	EXOC3	exocyst complex component 3	5
23293	SMG6	SMG6, nonsense mediated mRNA decay factor	5
7048	TGFBR2	transforming growth factor beta receptor 2	5
9094	UNC119	unc-119 lipid binding chaperone	5
2869	GRK5	G protein-coupled receptor kinase 5	5
8728	ADAM19	ADAM metallopeptidase domain 19	5
10800	CYSLTR1	cysteinyl leukotriene receptor 1	5
4088	SMAD3	SMAD family member 3	5
3927	LASP1	LIM and SH3 protein 1	5
178	AGL	amylo-alpha-1, 6-glucosidase, 4-alpha-glucanotransferase	5
25766	PRPF40B	pre-mRNA processing factor 40 homolog B	5
1455	CSNK1G2	casein kinase 1 gamma 2	5
5878	RAB5C	RAB5C, member RAS oncogene family	5
2997	GYS1	glycogen synthase 1	5
80152	CENPT	centromere protein T	5
940	CD28	CD28 molecule	5
79897	RPP21	ribonuclease P/MRP subunit p21	5
155061	ZNF746	zinc finger protein 746	5
6665	SOX15	SRY-box 15	5
79144	PPDPF	pancreatic progenitor cell differentiation and proliferation factor	5
169981	SPIN3	spindlin family member 3	5
23338	JADE2	jade family PHD finger 2	5
3707	ITPKB	inositol-trisphosphate 3-kinase B	5
9896	FIG4	FIG4 phosphoinositide 5-phosphatase	5
23144	ZC3H3	zinc finger CCCH-type containing 3	5
57479	PRR12	proline rich 12	5
9143	SYNGR3	synaptogyrin 3	5
80774	LIMD2	LIM domain containing 2	5
11337	GABARAP	GABA type A receptor-associated protein	5
54543	TOMM7	translocase of outer mitochondrial membrane 7	5
10567	RABAC1	Rab acceptor 1	5
64319	FBRS	fibrosin	5
6227	RPS21	ribosomal protein S21	5
29123	ANKRD11	ankyrin repeat domain 11	5
4041	LRP5	LDL receptor related protein 5	5
64375	IKZF4	IKAROS family zinc finger 4	5
100652768	LOC100652768	uncharacterized LOC100652768	5
6137	RPL13	ribosomal protein L13	5
219968	OR5B21	olfactory receptor family 5 subfamily B member 21	5
6135	RPL11	ribosomal protein L11	5
201163	FLCN	folliculin	5
100507347	VIM-AS1	VIM antisense RNA 1	5
57154	SMURF1	SMAD specific E3 ubiquitin protein ligase 1	5
5128	CDK17	cyclin dependent kinase 17	5
6208	RPS14	ribosomal protein S14	5
10169	SERF2	small EDRK-rich factor 2	5
4215	MAP3K3	mitogen-activated protein kinase kinase kinase 3	5
939	CD27	CD27 molecule	5

272	AMPD3	adenosine monophosphate deaminase 3	5
27287	VENTX	VENT homeobox	5
23094	SIPA1L3	signal induced proliferation associated 1 like 3	5
54463	FAM134B	family with sequence similarity 134 member B	5
57713	SFMBT2	Scm-like with four mbt domains 2	5
80003	PCNX2	pecanex homolog 2 (Drosophila)	5
22852	ANKRD26	ankyrin repeat domain 26	5
55626	AMBRA1	autophagy and beclin 1 regulator 1	5
5339	PLEC	plectin	5
55914	ERBIN	erbb2 interacting protein	5
5900	RALGDS	ral guanine nucleotide dissociation stimulator	5
23196	FAM120A	family with sequence similarity 120A	5
2634	GBP2	guanylate binding protein 2	5
6156	RPL30	ribosomal protein L30	5
246175	CNOT6L	CCR4-NOT transcription complex subunit 6 like	5
9806	SPOCK2	SPARC/osteonectin, cwcv and kazal like domains proteoglycan 2	5
29997	GLTSCR2	glioma tumor suppressor candidate region gene 2	5
5144	PDE4D	phosphodiesterase 4D	5
25976	TIPARP	TCDD inducible poly(ADP-ribose) polymerase	5
25865	PRKD2	protein kinase D2	5
4209	MEF2D	myocyte enhancer factor 2D	5
23077	MYCBP2	MYC binding protein 2, E3 ubiquitin protein ligase	5
57448	BIRC6	baculoviral IAP repeat containing 6	5
645843	TMEM14EP	transmembrane protein 14E, pseudogene	5
10326	SIRPB1	signal regulatory protein beta 1	5
55668	GPATCH2L	G-patch domain containing 2 like	5
81855	SFXN3	sideroflexin 3	5
9404	LPXN	leupaxin	5
6575	SLC20A2	solute carrier family 20 member 2	5
64748	PLPPR2	phospholipid phosphatase related 2	5
284346	ZNF575	zinc finger protein 575	5
55558	PLXNA3	plexin A3	5
646962	HRCT1	histidine rich carboxyl terminus 1	5
1564	CYP2D7	cytochrome P450 family 2 subfamily D member 7 (gene/pseudogene)	5
7094	TLN1	talin 1	5
130013	ACMSD	aminocarboxymuconate semialdehyde decarboxylase	5
57787	MARK4	microtubule affinity regulating kinase 4	5
55690	PACS1	phosphofurin acidic cluster sorting protein 1	5
81844	TRIM56	tripartite motif containing 56	5
196743	PAOX	polyamine oxidase	5
116985	ARAP1	ArfGAP with RhoGAP domain, ankyrin repeat and PH domain 1	5
65056	GPBP1	GC-rich promoter binding protein 1	5
84033	OBSCN	obscurin, cytoskeletal calmodulin and titin-interacting RhoGEF	5
283600	SLC25A47	solute carrier family 25 member 47	5
7291	TWIST1	twist family bHLH transcription factor 1	5
201294	UNC13D	unc-13 homolog D	5
100996693	LOC100996693	CAVP-target protein-like	5
64781	CERK	ceramide kinase	5
146206	CARMIL2	capping protein regulator and myosin 1 linker 2	5
653583	PHLDB3	pleckstrin homology like domain family B member 3	5
283385	MORN3	MORN repeat containing 3	5
352954	GATS	GATS, stromal antigen 3 opposite strand	5
7379	UPK2	uroplakin 2	5
29882	ANAPC2	anaphase promoting complex subunit 2	5
1535	CYBA	cytochrome b-245 alpha chain	5
5093	PCBP1	poly(rC) binding protein 1	5
79958	DENND1C	DENN domain containing 1C	5
79156	PLEKHF1	pleckstrin homology and FYVE domain containing 1	5
60684	TRAPPC11	trafficking protein particle complex 11	5
9821	RB1CC1	RB1 inducible coiled-coil 1	5
84256	FLYWCH1	FLYWCH-type zinc finger 1	5
51669	SARAF	store-operated calcium entry associated regulatory factor	5
51343	FZR1	fizzy/cell division cycle 20 related 1	5
8398	PLA2G6	phospholipase A2 group VI	5
54434	SSH1	slingshot protein phosphatase 1	5

2588	GALNS	galactosamine (N-acetyl)-6-sulfatase	5
399669	ZNF321P	zinc finger protein 321, pseudogene	5
2621	GAS6	growth arrest specific 6	5
57558	USP35	ubiquitin specific peptidase 35	5
284439	SLC25A42	solute carrier family 25 member 42	5
6181	RPLP2	ribosomal protein lateral stalk subunit P2	5
90625	ERVH48-1	endogenous retrovirus group 48 member 1	5
4753	NELL2	neural EGFL like 2	5
6222	RPS18	ribosomal protein S18	5
50840	TAS2R14	taste 2 receptor member 14	5
11215	AKAP11	A-kinase anchoring protein 11	5
81619	TSPAN14	tetraspanin 14	5
9448	MAP4K4	mitogen-activated protein kinase kinase kinase kinase 4	5
7750	ZMYM2	zinc finger MYM-type containing 2	5
10806	SDCCAG8	serologically defined colon cancer antigen 8	5
158078	EEF1A1P5	eukaryotic translation elongation factor 1 alpha 1 pseudogene 5	5
6228	RPS23	ribosomal protein S23	5
55423	SIRPG	signal regulatory protein gamma	5
919	CD247	CD247 molecule	5
1890	TYMP	thymidine phosphorylase	5
8553	BHLHE40	basic helix-loop-helix family member e40	5
162972	ZNF550	zinc finger protein 550	5
60401	EDA2R	ectodysplasin A2 receptor	5
192668	CYS1	cystin 1	5
57634	EP400	E1A binding protein p400	5
91252	SLC39A13	solute carrier family 39 member 13	5
11117	EMILIN1	elastin microfibril interfacer 1	5
51315	KRCC1	lysine rich coiled-coil 1	5
114132	SIGLEC11	sialic acid binding Ig like lectin 11	5
5498	PPOX	protoporphyrinogen oxidase	5
112574	SNX18	sorting nexin 18	5
58480	RHOU	ras homolog family member U	5
260425	MAGI3	membrane associated guanylate kinase, WW and PDZ domain containing 3	5
65998	C11orf95	chromosome 11 open reading frame 95	5
23743	BHMT2	betaine--homocysteine S-methyltransferase 2	5
23492	CBX7	chromobox 7	5
58509	CACTIN	cactin, spliceosome C complex subunit	5
27106	ARRDC2	arrestin domain containing 2	5
23053	ZSWIM8	zinc finger SWIM-type containing 8	5
1294	COL7A1	collagen type VII alpha 1 chain	5
79095	C9orf16	chromosome 9 open reading frame 16	5
7753	ZNF202	zinc finger protein 202	5
116535	MRGPRF	MAS related GPR family member F	5
5199	CFP	complement factor properdin	5
8792	TNFRSF11A	TNF receptor superfamily member 11a	5
259234	DSCR10	Down syndrome critical region 10 (non-protein coding)	5
6123	RPL3L	ribosomal protein L3 like	5
23352	UBR4	ubiquitin protein ligase E3 component n-recognin 4	5
375033	PEAR1	platelet endothelial aggregation receptor 1	5
10908	PNPLA6	patatin like phospholipase domain containing 6	5
22863	ATG14	autophagy related 14	5
4302	MLLT6	MLLT6, PHD finger domain containing	5
23265	EXOC7	exocyst complex component 7	5
1236	CCR7	C-C motif chemokine receptor 7	5
126393	HSPB6	heat shock protein family B (small) member 6	5
9701	PPP6R2	protein phosphatase 6 regulatory subunit 2	5
5075	PAX1	paired box 1	5
126282	TNFAIP8L1	TNF alpha induced protein 8 like 1	5
25950	RWDD3	RWD domain containing 3	5
146542	ZNF688	zinc finger protein 688	5
56124	PCDHB12	protocadherin beta 12	5
90987	ZNF251	zinc finger protein 251	5
101060376	TBC1D3L	TBC1 domain family member 3L	5
337867	UBAC2	UBA domain containing 2	5
678	ZFP36L2	ZFP36 ring finger protein like 2	5

6155	RPL27	ribosomal protein L27	5
924	CD7	CD7 molecule	5
5869	RAB5B	RAB5B, member RAS oncogene family	5
2687	GGT5	gamma-glutamyltransferase 5	5
3455	IFNAR2	interferon alpha and beta receptor subunit 2	5
55114	ARHGAP17	Rho GTPase activating protein 17	5
23300	ATMIN	ATM interactor	5
23157	SEPT6	septin 6	5
84433	CARD11	caspase recruitment domain family member 11	5
9363	RAB33A	RAB33A, member RAS oncogene family	5
23410	SIRT3	sirtuin 3	5
6141	RPL18	ribosomal protein L18	5
4092	SMAD7	SMAD family member 7	5
256281	NUDT14	nudix hydrolase 14	5
222234	FAM185A	family with sequence similarity 185 member A	5
126259	TMIGD2	transmembrane and immunoglobulin domain containing 2	5
84441	MAML2	mastermind like transcriptional coactivator 2	5
80162	PGGHG	protein-glucosylgalactosylhydroxylysine glucosidase	5
56995	TULP4	tubby like protein 4	5
5013	OTX1	orthodenticle homeobox 1	5
79818	ZNF552	zinc finger protein 552	5
4356	MPP3	membrane palmitoylated protein 3	5
23770	FKBP8	FK506 binding protein 8	5
346689	KLRG2	killer cell lectin like receptor G2	5
256021	LINC01619	long intergenic non-protein coding RNA 1619	5
9644	SH3PXD2A	SH3 and PX domains 2A	5
1384	CRAT	carnitine O-acetyltransferase	5
4925	NUCB2	nucleobindin 2	5
8839	WISP2	WNT1 inducible signaling pathway protein 2	5
27243	CHMP2A	charged multivesicular body protein 2A	5
5333	PLCD1	phospholipase C delta 1	5
309	ANXA6	annexin A6	5
3561	IL2RG	interleukin 2 receptor subunit gamma	5
79705	LRRK1	leucine rich repeat kinase 1	5
100874214	TM4SF19-AS1	TM4SF19 antisense RNA 1	5
200035	NUDT17	nudix hydrolase 17	5
3299	HSF4	heat shock transcription factor 4	5
974	CD79B	CD79b molecule	5
9423	NTN1	netrin 1	5
100128675	HPN-AS1	HPN antisense RNA 1	5
51005	AMDHD2	amidohydrolase domain containing 2	5
64806	IL25	interleukin 25	5
26127	FGFR1OP2	FGFR1 oncogene partner 2	5
101060684	NBPF26	neuroblastoma breakpoint family member 26	5
55204	GOLPH3L	golgi phosphoprotein 3 like	5
163087	ZNF383	zinc finger protein 383	5
83941	TM2D1	TM2 domain containing 1	5
10780	ZNF234	zinc finger protein 234	5
55844	PPP2R2D	protein phosphatase 2 regulatory subunit Bdelta	5
36	ACADSB	acyl-CoA dehydrogenase, short/branched chain	5
6342	SCP2	sterol carrier protein 2	5
219749	ZNF25	zinc finger protein 25	5
348094	ANKDD1A	ankyrin repeat and death domain containing 1A	5
51111	KMT5B	lysine methyltransferase 5B	5
55337	C19orf66	chromosome 19 open reading frame 66	5
1731	SEPT1	septin 1	5
11226	GALNT6	polypeptide N-acetylgalactosaminyltransferase 6	5
55900	ZNF302	zinc finger protein 302	5
132160	PPM1M	protein phosphatase, Mg2+/Mn2+ dependent 1M	5
6775	STAT4	signal transducer and activator of transcription 4	5
28951	TRIB2	tribbles pseudokinase 2	5
1891	ECH1	enoyl-CoA hydratase 1	5
8195	MKKS	McKusick-Kaufman syndrome	5
388969	C2orf68	chromosome 2 open reading frame 68	5
9087	TMSB4Y	thymosin beta 4, Y-linked	5

51247	PAIP2	poly(A) binding protein interacting protein 2	5
11060	WWP2	WW domain containing E3 ubiquitin protein ligase 2	5
8434	RECK	reversion inducing cysteine rich protein with kazal motifs	5
5412	UBL3	ubiquitin like 3	5
55501	CHST12	carbohydrate sulfotransferase 12	5
83463	MXD3	MAX dimerization protein 3	5
55251	PCMTD2	protein-L-isoaspartate (D-aspartate) O-methyltransferase domain containing 2	5
115817	DHRS1	dehydrogenase/reductase 1	5
10916	MAGED2	MAGE family member D2	5
26152	ZNF337	zinc finger protein 337	5
6158	RPL28	ribosomal protein L28	5
54532	USP53	ubiquitin specific peptidase 53	5
1195	CLK1	CDC like kinase 1	5
55219	TMEM57	transmembrane protein 57	5
2778	GNAS	GNAS complex locus	5
9746	CLSTN3	calsyntenin 3	5
23523	CABIN1	calcineurin binding protein 1	5
100131187	TSTD1	thiosulfate sulfurtransferase like domain containing 1	5
4007	PRICKLE3	prickle planar cell polarity protein 3	5
339366	ADAMTSL5	ADAMTS like 5	5
10045	SH2D3A	SH2 domain containing 3A	5
79132	DHX58	DEXH-box helicase 58	5
9522	SCAMP1	secretory carrier membrane protein 1	5
11179	ZNF277	zinc finger protein 277	5
4926	NUMA1	nuclear mitotic apparatus protein 1	5
390927	ZNF793	zinc finger protein 793	5
729238	SFTPA2	surfactant protein A2	5
57132	CHMP1B	charged multivesicular body protein 1B	5
56925	LXN	latexin	5
3590	IL11RA	interleukin 11 receptor subunit alpha	5
474344	GIMAP6	GTPase, IMAP family member 6	5
1794	DOCK2	dedicator of cytokinesis 2	5
255967	PAN3	PAN3 poly(A) specific ribonuclease subunit	5
4627	MYH9	myosin heavy chain 9	5
55187	VPS13D	vacuolar protein sorting 13 homolog D	5
80325	ABTB1	ankyrin repeat and BTB domain containing 1	5
8764	TNFRSF14	TNF receptor superfamily member 14	5
23503	ZFYVE26	zinc finger FYVE-type containing 26	5
9969	MED13	mediator complex subunit 13	5
23230	VPS13A	vacuolar protein sorting 13 homolog A	5
9354	UBE4A	ubiquitination factor E4A	5
22992	KDM2A	lysine demethylase 2A	5
113	ADCY7	adenylate cyclase 7	5
5289	PIK3C3	phosphatidylinositol 3-kinase catalytic subunit type 3	5
7155	TOP2B	topoisomerase (DNA) II beta	5
6942	TCF20	transcription factor 20	5
2316	FLNA	filamin A	5
23550	PSD4	pleckstrin and Sec7 domain containing 4	5
50839	TAS2R10	taste 2 receptor member 10	5
23215	PRRC2C	proline rich coiled-coil 2C	5
10838	ZNF275	zinc finger protein 275	5
256364	EML3	echinoderm microtubule associated protein like 3	5
56252	YLPM1	YLP motif containing 1	5
25792	CIZ1	CDKN1A interacting zinc finger protein 1	5
126374	WTIP	Wilms tumor 1 interacting protein	5
147686	ZNF418	zinc finger protein 418	5
23005	MAPKBP1	mitogen-activated protein kinase binding protein 1	5
129530	LYG1	lysozyme g1	5
64772	ENGASE	endo-beta-N-acetylglucosaminidase	5
5585	PKN1	protein kinase N1	5
114904	C1QTNF6	C1q and tumor necrosis factor related protein 6	5
80320	SP6	Sp6 transcription factor	5
63941	NECAB3	N-terminal EF-hand calcium binding protein 3	5
8547	FCN3	ficolin 3	5
115196	ZNF554	zinc finger protein 554	5

7786	MAP3K12	mitogen-activated protein kinase kinase kinase 12	5
673	BRAF	B-Raf proto-oncogene, serine/threonine kinase	5
290	ANPEP	alanyl aminopeptidase, membrane	5
64760	FAM160B2	family with sequence similarity 160 member B2	5
51043	ZBTB7B	zinc finger and BTB domain containing 7B	5
100126793	GHRLOS	ghrelin opposite strand/antisense RNA	5
23002	DAAM1	dishevelled associated activator of morphogenesis 1	5
9202	ZMYM4	zinc finger MYM-type containing 4	5
6651	SON	SON DNA binding protein	5
55209	SETD5	SET domain containing 5	5
23592	LEMD3	LEM domain containing 3	5
57683	ZDBF2	zinc finger DBF-type containing 2	5
5062	PAK2	p21 (RAC1) activated kinase 2	5
259282	BOD1L1	biorientation of chromosomes in cell division 1 like 1	5
10396	ATP8A1	ATPase phospholipid transporting 8A1	5
282809	POC1B	POC1 centriolar protein B	5
63908	NAPB	NSF attachment protein beta	5
284459	HKR1	HKR1, GLI-Kruppel zinc finger family member	5
7392	USF2	upstream transcription factor 2, c-fos interacting	5
221037	JMJD1C	jumonji domain containing 1C	5
3423	IDS	iduronate 2-sulfatase	5
26020	LRP10	LDL receptor related protein 10	5
91748	ELMSAN1	ELM2 and Myb/SANT domain containing 1	5
51177	PLEKHO1	pleckstrin homology domain containing O1	5
4736	RPL10A	ribosomal protein L10a	5
23262	PPIP5K2	diphosphoinositol pentakisphosphate kinase 2	5
22980	TCF25	transcription factor 25	5
118924	FRA10AC1	fragile site, folic acid type, rare, fra(10)(q23.3) or fra(10)(q24.2) candidate 1	5
23461	ABCA5	ATP binding cassette subfamily A member 5	5
57189	KIAA1147	KIAA1147	5
8085	KMT2D	lysine methyltransferase 2D	5
26235	FBXL4	F-box and leucine rich repeat protein 4	5
23162	MAPK8IP3	mitogen-activated protein kinase 8 interacting protein 3	5
23067	SETD1B	SET domain containing 1B	5
200539	ANKRD23	ankyrin repeat domain 23	5
23315	SLC9A8	solute carrier family 9 member A8	5
55125	CEP192	centrosomal protein 192	5
489	ATP2A3	ATPase sarcoplasmic/endoplasmic reticulum Ca2+ transporting 3	5
83931	STK40	serine/threonine kinase 40	5
730094	C16orf52	chromosome 16 open reading frame 52	5
4899	NRF1	nuclear respiratory factor 1	5
50832	TAS2R4	taste 2 receptor member 4	5
26190	FBXW2	F-box and WD repeat domain containing 2	5
55827	DCAF6	DDB1 and CUL4 associated factor 6	5
27030	MLH3	mutL homolog 3	5
7620	ZNF69	zinc finger protein 69	5
126069	ZNF491	zinc finger protein 491	5
221496	LEMD2	LEM domain containing 2	5
55454	CSGALNACT2	chondroitin sulfate N-acetylgalactosaminyltransferase 2	5
85377	MICALL1	MICAL like 1	5
80208	SPG11	spastic paraplegia 11 (autosomal recessive)	5
57614	KIAA1468	KIAA1468	5
25836	NIPBL	NIPBL, cohesin loading factor	5
54799	MBTD1	mbt domain containing 1	5
10009	ZBTB33	zinc finger and BTB domain containing 33	5
54681	P4HTM	prolyl 4-hydroxylase, transmembrane	5
55139	ANKZF1	ankyrin repeat and zinc finger domain containing 1	5
81932	HDHD3	haloacid dehalogenase like hydrolase domain containing 3	5
8924	HERC2	HECT and RLD domain containing E3 ubiquitin protein ligase 2	5
26260	FBXO25	F-box protein 25	5
51755	CDK12	cyclin dependent kinase 12	5
9205	ZMYM5	zinc finger MYM-type containing 5	5
257218	SHPRH	SNF2 histone linker PHD RING helicase	5
7073	TIAL1	TIA1 cytotoxic granule associated RNA binding protein like 1	5
57148	RALGAPB	Ral GTPase activating protein non-catalytic beta subunit	5

3213	HOXB3	homeobox B3	5
23637	RABGAP1	RAB GTPase activating protein 1	5
339345	NANOS2	nanos C2HC-type zinc finger 2	5
100507424	LOC100507424	uncharacterized LOC100507424	5
642819	ZNF487	zinc finger protein 487	5
8419	BFSP2	beaded filament structural protein 2	5
1185	CLCN6	chloride voltage-gated channel 6	5
84527	ZNF559	zinc finger protein 559	5
388564	TMEM238	transmembrane protein 238	5
51105	PHF20L1	PHD finger protein 20-like 1	5
317662	FAM149B1	family with sequence similarity 149 member B1	5
8481	OFD1	OFD1, centriole and centriolar satellite protein	5
89857	KLHL6	kelch like family member 6	5
27125	AFF4	AF4/FMR2 family member 4	5
7464	CORO2A	coronin 2A	5
51304	ZDHHC3	zinc finger DHHC-type containing 3	5
57690	TNRC6C	trinucleotide repeat containing 6C	5
83692	CD99L2	CD99 molecule like 2	5
50488	MINK1	misshapen like kinase 1	5
55054	ATG16L1	autophagy related 16 like 1	5
55683	KANSL3	KAT8 regulatory NSL complex subunit 3	5
5991	RFX3	regulatory factor X3	5
3570	IL6R	interleukin 6 receptor	5
54	ACP5	acid phosphatase 5, tartrate resistant	5
160851	DGKH	diacylglycerol kinase eta	5
84914	ZNF587	zinc finger protein 587	5
22933	SIRT2	sirtuin 2	5
652968	GATSL3	GATS protein like 3	5
196403	DTX3	deltex E3 ubiquitin ligase 3	5
51191	HERC5	HECT and RLD domain containing E3 ubiquitin protein ligase 5	5
57498	KIDINS220	kinase D-interacting substrate 220kDa	5
1389	CREBL2	cAMP responsive element binding protein like 2	5
9980	DOPEY2	dopey family member 2	5
8543	LMO4	LIM domain only 4	5
91782	CHMP7	charged multivesicular body protein 7	5
5530	PPP3CA	protein phosphatase 3 catalytic subunit alpha	5
9847	C2CD5	C2 calcium dependent domain containing 5	5
149041	RC3H1	ring finger and CCCH-type domains 1	5
5025	P2RX4	purinergic receptor P2X 4	5
29068	ZBTB44	zinc finger and BTB domain containing 44	5
10585	POMT1	protein O-mannosyltransferase 1	5
3140	MR1	major histocompatibility complex, class I-related	5
8556	CDC14A	cell division cycle 14A	5
54981	NMRK1	nicotinamide riboside kinase 1	5
117584	RFFL	ring finger and FYVE like domain containing E3 ubiquitin protein ligase	5
841	CASP8	caspase 8	5
1387	CREBBP	CREB binding protein	5
10347	ABCA7	ATP binding cassette subfamily A member 7	5
4820	NKTR	natural killer cell triggering receptor	5
2323	FLT3LG	fms related tyrosine kinase 3 ligand	5
274	BIN1	bridging integrator 1	5
80830	APOL6	apolipoprotein L6	5
54904	WHSC1L1	Wolf-Hirschhorn syndrome candidate 1-like 1	5
6314	ATXN7	ataxin 7	5
8861	LDB1	LIM domain binding 1	5
5829	PXN	paxillin	5
58485	TRAPPC1	trafficking protein particle complex 1	5
10044	SH2D3C	SH2 domain containing 3C	5
143098	MPP7	membrane palmitoylated protein 7	5
11123	RCAN3	RCAN family member 3	5
4046	LSP1	lymphocyte-specific protein 1	5
6404	SELPLG	selectin P ligand	5
51585	PCF11	PCF11 cleavage and polyadenylation factor subunit	5
3338	DNAJC4	DnaJ heat shock protein family (Hsp40) member C4	5
123036	TC2N	tandem C2 domains, nuclear	5

53822	FXYD7	FXYD domain containing ion transport regulator 7	5
51411	BIN2	bridging integrator 2	5
79932	KIAA0319L	KIAA0319 like	5
25939	SAMHD1	SAM and HD domain containing deoxynucleoside triphosphate triphosphohydrolase 1	5
11342	RNF13	ring finger protein 13	5
53346	TM6SF1	transmembrane 6 superfamily member 1	5
10559	SLC35A1	solute carrier family 35 member A1	5
900	CCNG1	cyclin G1	5
84851	TRIM52	tripartite motif containing 52	5
84958	SYTL1	synaptotagmin like 1	5
9840	TESPA1	thymocyte expressed, positive selection associated 1	5
4050	LTB	lymphotoxin beta	5
150365	MEI1	meiotic double-stranded break formation protein 1	5
54847	SIDT1	SID1 transmembrane family member 1	5
11010	GLIPR1	GLI pathogenesis related 1	5
284129	SLC26A11	solute carrier family 26 member 11	5
837	CASP4	caspase 4	5
54622	ARL15	ADP ribosylation factor like GTPase 15	5
5527	PPP2R5C	protein phosphatase 2 regulatory subunit B'gamma	5
91523	PCED1B	PC-esterase domain containing 1B	5
3135	HLA-G	major histocompatibility complex, class I, G	5
91689	SMDT1	single-pass membrane protein with aspartate rich tail 1	5
23125	CAMTA2	calmodulin binding transcription activator 2	5
5920	RARRES3	retinoic acid receptor responder 3	5
3594	IL12RB1	interleukin 12 receptor subunit beta 1	5
360	AQP3	aquaporin 3 (Gill blood group)	5
158830	CXorf65	chromosome X open reading frame 65	5
3955	LFNG	LFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase	5
57489	ODF2L	outer dense fiber of sperm tails 2 like	5
7567	ZNF19	zinc finger protein 19	5
219402	MTIF3	mitochondrial translational initiation factor 3	5
123688	HYKK	hydroxylysine kinase	5
5588	PRKCQ	protein kinase C theta	5
6275	S100A4	S100 calcium binding protein A4	5
118429	ANTXR2	anthrax toxin receptor 2	5
177	AGER	advanced glycosylation end-product specific receptor	5
10365	KLF2	Kruppel like factor 2	5
51274	KLF3	Kruppel like factor 3	5
2537	IFI6	interferon alpha inducible protein 6	5
4063	LY9	lymphocyte antigen 9	5
201595	STT3B	STT3B, catalytic subunit of the oligosaccharyltransferase complex	5
151613	TTC14	tetratricopeptide repeat domain 14	5
9725	TMEM63A	transmembrane protein 63A	5
51586	MED15	mediator complex subunit 15	5
23515	MORC3	MORC family CW-type zinc finger 3	5
23046	KIF21B	kinesin family member 21B	5
2145	EZH1	enhancer of zeste 1 polycomb repressive complex 2 subunit	5
5175	PECAM1	platelet and endothelial cell adhesion molecule 1	5
387357	THEMIS	thymocyte selection associated	5
29767	TMOD2	tropomodulin 2	5
4599	MX1	MX dynamin like GTPase 1	5
916	CD3E	CD3e molecule	5
972	CD74	CD74 molecule	5
220972	MARCH8	membrane associated ring-CH-type finger 8	5
115209	OMA1	OMA1 zinc metallopeptidase	5
84456	L3MBTL3	l(3)mbt-like 3 (Drosophila)	5
4179	CD46	CD46 molecule	5
51816	CECR1	cat eye syndrome chromosome region, candidate 1	5
51019	CCDC53	coiled-coil domain containing 53	5
196513	DCP1B	decapping mRNA 1B	5
23593	HEBP2	heme binding protein 2	5
10627	MYL12A	myosin light chain 12A	5
55217	TMLHE	trimethyllysine hydroxylase, epsilon	5
55281	TMEM140	transmembrane protein 140	5
5371	PML	promyelocytic leukemia	5

55906	ZC4H2	zinc finger C4H2-type containing	5
9113	LATS1	large tumor suppressor kinase 1	5
4494	MT1F	metallothionein 1F	5
389289	ANXA2R	annexin A2 receptor	5
22884	WDR37	WD repeat domain 37	5
6430	SRSF5	serine and arginine rich splicing factor 5	5
317649	EIF4E3	eukaryotic translation initiation factor 4E family member 3	5
94241	TP53INP1	tumor protein p53 inducible nuclear protein 1	5
93550	ZFAND4	zinc finger AN1-type containing 4	5
10397	NDRG1	N-myc downstream regulated 1	5
8916	HERC3	HECT and RLD domain containing E3 ubiquitin protein ligase 3	5
6903	TBCC	tubulin folding cofactor C	5
301	ANXA1	annexin A1	5
79726	WDR59	WD repeat domain 59	5
159090	FAM122B	family with sequence similarity 122B	5
284004	HEXDC	hexosaminidase D	5
10781	ZNF266	zinc finger protein 266	5
151636	DTX3L	deltex E3 ubiquitin ligase 3L	5
7507	XPA	XPA, DNA damage recognition and repair factor	5
23287	AGTPBP1	ATP/GTP binding protein 1	5
146198	ZFP90	ZFP90 zinc finger protein	5
405	ARNT	aryl hydrocarbon receptor nuclear translocator	5
9867	PJA2	praja ring finger ubiquitin ligase 2	5
79364	ZXDC	ZXD family zinc finger C	5
158219	TTC39B	tetratricopeptide repeat domain 39B	5
221178	SPATA13	spermatogenesis associated 13	5
128346	C1orf162	chromosome 1 open reading frame 162	5
9267	CYTH1	cytohesin 1	5
3431	SP110	SP110 nuclear body protein	5
157378	TMEM65	transmembrane protein 65	5
152926	PPM1K	protein phosphatase, Mg2+/Mn2+ dependent 1K	5
5775	PTPN4	protein tyrosine phosphatase, non-receptor type 4	5
92797	HELB	DNA helicase B	5
81704	DOCK8	dedicator of cytokinesis 8	5
29909	GPR171	G protein-coupled receptor 171	5
147138	TMC8	transmembrane channel like 8	5
10466	COG5	component of oligomeric golgi complex 5	5
6667	SP1	Sp1 transcription factor	5
8554	PIAS1	protein inhibitor of activated STAT 1	5
757	TMEM50B	transmembrane protein 50B	5
55825	PECR	peroxisomal trans-2-enoyl-CoA reductase	5
493	ATP2B4	ATPase plasma membrane Ca2+ transporting 4	5
3655	ITGA6	integrin subunit alpha 6	5
5292	PIM1	Pim-1 proto-oncogene, serine/threonine kinase	5
9922	IQSEC1	IQ motif and Sec7 domain 1	5
152006	RNF38	ring finger protein 38	5
163049	ZNF791	zinc finger protein 791	5
4214	MAP3K1	mitogen-activated protein kinase kinase kinase 1	5
23032	USP33	ubiquitin specific peptidase 33	5
23033	DOPEY1	dopey family member 1	5
56605	ERO1B	endoplasmic reticulum oxidoreductase 1 beta	5
27430	MAT2B	methionine adenosyltransferase 2B	5
388558	ZNF808	zinc finger protein 808	5
8867	SYNJ1	synaptojanin 1	5
84719	LINC00260	long intergenic non-protein coding RNA 260	5
51667	NUB1	negative regulator of ubiquitin like proteins 1	5
79770	TXNDC15	thioredoxin domain containing 15	5
834	CASP1	caspase 1	5
64598	MOSPD3	motile sperm domain containing 3	5
3106	HLA-B	major histocompatibility complex, class I, B	5
3669	ISG20	interferon stimulated exonuclease gene 20	5
554223	LOC554223	histocompatibility antigen-related	5
4077	NBR1	NBR1, autophagy cargo receptor	5
10379	IRF9	interferon regulatory factor 9	5
64844	MARCH7	membrane associated ring-CH-type finger 7	5

3841	KPNA5	karyopherin subunit alpha 5	5
8644	AKR1C3	aldo-keto reductase family 1 member C3	5
54464	XRN1	5'-3' exoribonuclease 1	5
80342	TRAF3IP3	TRAF3 interacting protein 3	5
5335	PLCG1	phospholipase C gamma 1	5
55007	FAM118A	family with sequence similarity 118 member A	5
26999	CYFIP2	cytoplasmic FMR1 interacting protein 2	5
51478	HSD17B7	hydroxysteroid 17-beta dehydrogenase 7	5
91351	DDX60L	DEAD-box helicase 60-like	5
9445	ITM2B	integral membrane protein 2B	5
388552	BLOC1S3	biogenesis of lysosomal organelles complex 1 subunit 3	5
54809	SAMD9	sterile alpha motif domain containing 9	5
219285	SAMD9L	sterile alpha motif domain containing 9 like	5
80833	APOL3	apolipoprotein L3	5
3581	IL9R	interleukin 9 receptor	5
1519	CTSO	cathepsin O	5
63935	PCIF1	PDX1 C-terminal inhibiting factor 1	5
8615	USO1	USO1 vesicle transport factor	5
1655	DDX5	DEAD-box helicase 5	5
28968	SLC6A16	solute carrier family 6 member 16	5
6786	STIM1	stromal interaction molecule 1	5
57018	CCNL1	cyclin L1	5
10455	ECI2	enoyl-CoA delta isomerase 2	5
7597	ZBTB25	zinc finger and BTB domain containing 25	5
114769	CARD16	caspase recruitment domain family member 16	5
54891	INO80D	INO80 complex subunit D	5
8875	VNN2	vanin 2	5
162394	SLFN5	schlafen family member 5	5
55196	KIAA1551	KIAA1551	5
397	ARHGDIB	Rho GDP dissociation inhibitor beta	5
91526	ANKRD44	ankyrin repeat domain 44	5
5934	RBL2	RB transcriptional corepressor like 2	5
23586	DDX58	DEXD/H-box helicase 58	5
1388	ATF6B	activating transcription factor 6 beta	5
10521	DDX17	DEAD-box helicase 17	5
64771	C6orf106	chromosome 6 open reading frame 106	5
89848	FCHSD1	FCH and double SH3 domains 1	5
9881	TRANK1	tetratricopeptide repeat and ankyrin repeat containing 1	5
3275	PRMT2	protein arginine methyltransferase 2	5
7059	THBS3	thrombospondin 3	5
9976	CLEC2B	C-type lectin domain family 2 member B	5
832	CAPZB	capping actin protein of muscle Z-line beta subunit	5
79903	NAA60	N(alpha)-acetyltransferase 60, NatF catalytic subunit	5
57097	PARP11	poly(ADP-ribose) polymerase family member 11	5
51000	SLC35B3	solute carrier family 35 member B3	5
2633	GBP1	guanylate binding protein 1	5
112849	L3HYPDH	trans-L-3-hydroxyproline dehydratase	5
901	CCNG2	cyclin G2	5
1429	CRYZ	crystallin zeta	5
3105	HLA-A	major histocompatibility complex, class I, A	5
94240	EPSTI1	epithelial stromal interaction 1 (breast)	5
3134	HLA-F	major histocompatibility complex, class I, F	5
11119	BTN3A1	butyrophilin subfamily 3 member A1	5
3139	HLA-L	major histocompatibility complex, class I, L (pseudogene)	5
10161	LPAR6	lysophosphatidic acid receptor 6	5
10154	PLXNC1	plexin C1	5
79603	CERS4	ceramide synthase 4	5
84173	ELMOD3	ELMO domain containing 3	5
55837	EAPP	E2F associated phosphoprotein	5
3107	HLA-C	major histocompatibility complex, class I, C	5
222223	KIAA1324L	KIAA1324 like	5
49855	SCAPER	S-phase cyclin A associated protein in the ER	5
64386	MMP25	matrix metallopeptidase 25	5
7538	ZFP36	ZFP36 ring finger protein	5
55437	STRADB	STE20-related kinase adaptor beta	5

80298	MTERF2	mitochondrial transcription termination factor 2	5
1025	CDK9	cyclin dependent kinase 9	5
4943	TBC1D25	TBC1 domain family member 25	5
90826	PRMT9	protein arginine methyltransferase 9	5
54497	HEATR5B	HEAT repeat containing 5B	5
22878	TRAPPC8	trafficking protein particle complex 8	5
1513	CTSK	cathepsin K	5
79654	HECTD3	HECT domain E3 ubiquitin protein ligase 3	5
8450	CUL4B	cullin 4B	5
27241	BBS9	Bardet-Biedl syndrome 9	5
23060	ZNF609	zinc finger protein 609	5
8816	DCAF5	DDB1 and CUL4 associated factor 5	5
84727	SPSB2	splA/ryanodine receptor domain and SOCS box containing 2	5
51379	CRLF3	cytokine receptor like factor 3	5
3071	NCKAP1L	NCK associated protein 1 like	5
55288	RHOT1	ras homolog family member T1	5
10444	ZER1	zyg-11 related cell cycle regulator	5
842	CASP9	caspase 9	5
92	ACVR2A	activin A receptor type 2A	5
4690	NCK1	NCK adaptor protein 1	5
84307	ZNF397	zinc finger protein 397	5
7716	VEZF1	vascular endothelial zinc finger 1	5
64091	POPDC2	popeye domain containing 2	5
8934	RAB29	RAB29, member RAS oncogene family	5
55283	MCOLN3	mucolipin 3	5
23588	KLHDC2	kelch domain containing 2	5
4600	MX2	MX dynamin like GTPase 2	5
9860	LRIG2	leucine rich repeats and immunoglobulin like domains 2	5
7852	CXCR4	C-X-C motif chemokine receptor 4	5
64109	CRLF2	cytokine receptor-like factor 2	5
9528	TMEM59	transmembrane protein 59	5
2319	FLOT2	flotillin 2	5
686	BTD	biotinidase	5
7046	TGFBR1	transforming growth factor beta receptor 1	5
3903	LAIR1	leukocyte associated immunoglobulin like receptor 1	5
22821	RASA3	RAS p21 protein activator 3	5
55070	DET1	de-etiolated homolog 1 (Arabidopsis)	5
57184	FAM219B	family with sequence similarity 219 member B	5
153241	CEP120	centrosomal protein 120	5
25809	TTLL1	tubulin tyrosine ligase like 1	5
55762	ZNF701	zinc finger protein 701	5
22841	RAB11FIP2	RAB11 family interacting protein 2	5
119504	ANAPC16	anaphase promoting complex subunit 16	5
286530	P2RY8	purinergic receptor P2Y8	5
55080	TAPBPL	TAP binding protein like	5
6746	SSR2	signal sequence receptor subunit 2	5
54103	GSAP	gamma-secretase activating protein	5
79991	OBFC1	oligonucleotide/oligosaccharide binding fold containing 1	5
51170	HSD17B11	hydroxysteroid 17-beta dehydrogenase 11	5
79758	DHRS12	dehydrogenase/reductase 12	5
283897	C16orf54	chromosome 16 open reading frame 54	5
29978	UBQLN2	ubiquilin 2	5
139716	GAB3	GRB2 associated binding protein 3	5
6619	SNAPC3	small nuclear RNA activating complex polypeptide 3	5
53347	UBASH3A	ubiquitin associated and SH3 domain containing A	5
57763	ANKRA2	ankyrin repeat family A member 2	5
6095	RORA	RAR related orphan receptor A	5
6777	STAT5B	signal transducer and activator of transcription 5B	5
7182	NR2C2	nuclear receptor subfamily 2 group C member 2	5
85007	PHYKPL	5-phosphohydroxy-L-lysine phospho-lyase	5
84765	ZNF577	zinc finger protein 577	5
10144	FAM13A	family with sequence similarity 13 member A	5
1154	CISH	cytokine inducible SH2 containing protein	5
64418	TMEM168	transmembrane protein 168	5
4689	NCF4	neutrophil cytosolic factor 4	5

1520	CTSS	cathepsin S	5
59307	SIGIRR	single Ig and TIR domain containing	5
11329	STK38	serine/threonine kinase 38	5
54440	SASH3	SAM and SH3 domain containing 3	5
545	ATR	ATR serine/threonine kinase	5
7693	ZNF134	zinc finger protein 134	5
10947	AP3M2	adaptor related protein complex 3 mu 2 subunit	5
728743	LOC728743	zinc finger protein pseudogene	5
7311	UBA52	ubiquitin A-52 residue ribosomal protein fusion product 1	5
55357	TBC1D2	TBC1 domain family member 2	5
6468	FBXW4	F-box and WD repeat domain containing 4	5
8698	S1PR4	sphingosine-1-phosphate receptor 4	5
204851	HIPK1	homeodomain interacting protein kinase 1	5
54778	RNF111	ring finger protein 111	5
84532	ACSS1	acyl-CoA synthetase short-chain family member 1	5
80335	WDR82	WD repeat domain 82	5
9905	SGSM2	small G protein signaling modulator 2	5
4242	MFNG	MFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase	5
388324	INCA1	inhibitor of CDK, cyclin A1 interacting protein 1	5
57567	ZNF319	zinc finger protein 319	5
25992	SNED1	sushi, nidogen and EGF like domains 1	5
79717	PPCS	phosphopantothenoylcysteine synthetase	5
51091	SEPSECS	Sep (O-phosphoserine) tRNA:Sec (selenocysteine) tRNA synthase	5
55846	ITFG2	integrin alpha FG-GAP repeat containing 2	5
64174	DPEP2	dipeptidase 2	5
9834	FAM30A	family with sequence similarity 30, member A	5
24142	NAT6	N-acetyltransferase 6	5
57181	SLC39A10	solute carrier family 39 member 10	5
374986	MIGA1	mitoguardin 1	5
847	CAT	catalase	5
9842	PLEKHM1	pleckstrin homology and RUN domain containing M1	5
66035	SLC2A11	solute carrier family 2 member 11	5
6872	TAF1	TATA-box binding protein associated factor 1	5
80230	RUFY1	RUN and FYVE domain containing 1	5
259290	TAS2R31	taste 2 receptor member 31	5
51291	GMIP	GEM interacting protein	5
25900	IFFO1	intermediate filament family orphan 1	5
9736	USP34	ubiquitin specific peptidase 34	5
5494	PPM1A	protein phosphatase, Mg2+/Mn2+ dependent 1A	5
83874	TBC1D10A	TBC1 domain family member 10A	5
5287	PIK3C2B	phosphatidylinositol-4-phosphate 3-kinase catalytic subunit type 2 beta	5
53373	TPCN1	two pore segment channel 1	5
96459	FNIP1	folliculin interacting protein 1	5
51592	TRIM33	tripartite motif containing 33	5
8720	MBTPS1	membrane bound transcription factor peptidase, site 1	5
23167	EFR3A	EFR3 homolog A	5
221491	C6orf1	chromosome 6 open reading frame 1	5
887	CCKBR	cholecystokinin B receptor	5
1509	CTSD	cathepsin D	5
283149	BCL9L	B-cell CLL/lymphoma 9-like	5
6239	RREB1	ras responsive element binding protein 1	5
6497	SKI	SKI proto-oncogene	5
7745	ZKSCAN8	zinc finger with KRAB and SCAN domains 8	5
23389	MED13L	mediator complex subunit 13 like	5
8289	ARID1A	AT-rich interaction domain 1A	5
324	APC	APC, WNT signaling pathway regulator	5
4750	NEK1	NIMA related kinase 1	5
89845	ABCC10	ATP binding cassette subfamily C member 10	5
5058	PAK1	p21 (RAC1) activated kinase 1	5
4680	CEACAM6	carcinoembryonic antigen related cell adhesion molecule 6	5
1773	DNASE1	deoxyribonuclease 1	5
64219	PJA1	praja ring finger ubiquitin ligase 1	5
23339	VPS39	VPS39, HOPS complex subunit	5
57610	RANBP10	RAN binding protein 10	5
80124	VCPIP1	valosin containing protein interacting protein 1	5

143	PARP4	poly(ADP-ribose) polymerase family member 4	5
9682	KDM4A	lysine demethylase 4A	5
55088	CCDC186	coiled-coil domain containing 186	5
23398	PPWD1	peptidylprolyl isomerase domain and WD repeat containing 1	5
59348	ZNF350	zinc finger protein 350	5
57674	RNF213	ring finger protein 213	5
9583	ENTPD4	ectonucleoside triphosphate diphosphohydrolase 4	5
100506736	SLFN12L	schlafen family member 12 like	5
55667	DENND4C	DENN domain containing 4C	5
123283	TARSL2	threonyl-tRNA synthetase like 2	5
843	CASP10	caspase 10	5
102724748	LOC102724748	uncharacterized LOC102724748	5
100506639	LOC100506639	uncharacterized LOC100506639	5
7328	UBE2H	ubiquitin conjugating enzyme E2 H	5
9168	TMSB10	thymosin beta 10	5
84861	KLHL22	kelch like family member 22	5
26157	GIMAP2	GTPase, IMAP family member 2	5
8445	DYRK2	dual specificity tyrosine phosphorylation regulated kinase 2	5
80256	FAM214B	family with sequence similarity 214 member B	5
116843	SLC18B1	solute carrier family 18 member B1	5
10077	TSPAN32	tetraspanin 32	5
4189	DNAJB9	DnaJ heat shock protein family (Hsp40) member B9	5
100505761	RPARP-AS1	RPARP antisense RNA 1	5
79573	TTC13	tetratricopeptide repeat domain 13	5
9214	FCMR	Fc fragment of IgM receptor	5
84265	POLR3GL	RNA polymerase III subunit G like	5
6167	RPL37	ribosomal protein L37	5
79722	ANKRD55	ankyrin repeat domain 55	5
130814	PQLC3	PQ loop repeat containing 3	5
9692	KIAA0391	KIAA0391	5
51449	PCYOX1	prenylcysteine oxidase 1	5
64919	BCL11B	B-cell CLL/lymphoma 11B	5
84264	HAGHL	hydroxyacylglutathione hydrolase-like	5
221908	PPP1R35	protein phosphatase 1 regulatory subunit 35	5
125958	OR7D4	olfactory receptor family 7 subfamily D member 4	5
6169	RPL38	ribosomal protein L38	5
116093	DIRC1	disrupted in renal carcinoma 1	5
57719	ANO8	anoctamin 8	5
283726	SAXO2	stabilizer of axonemal microtubules 2	5
11156	PTP4A3	protein tyrosine phosphatase type IVA, member 3	5
58473	PLEKHB1	pleckstrin homology domain containing B1	5
92714	ARRDC1	arrestin domain containing 1	5
55707	NECAP2	NECAP endocytosis associated 2	5
79699	ZYG11B	zyg-11 family member B, cell cycle regulator	5
5465	PPARA	peroxisome proliferator activated receptor alpha	5
54916	TMEM260	transmembrane protein 260	5
283232	TMEM80	transmembrane protein 80	5
285268	ZNF621	zinc finger protein 621	5
57194	ATP10A	ATPase phospholipid transporting 10A (putative)	5
63035	BCORL1	BCL6 corepressor-like 1	5
321	APBA2	amyloid beta precursor protein binding family A member 2	5
9919	SEC16A	SEC16 homolog A, endoplasmic reticulum export factor	5
56242	ZNF253	zinc finger protein 253	5
10235	RASGRP2	RAS guanyl releasing protein 2	5
9827	RGP1	RGP1 homolog, RAB6A GEF complex partner 1	5
7673	ZNF222	zinc finger protein 222	5
51279	C1RL	complement C1r subcomponent like	5
84925	DIRC2	disrupted in renal carcinoma 2	5
10801	SEPT9	septin 9	5
51763	INPP5K	inositol polyphosphate-5-phosphatase K	5
22864	R3HDM2	R3H domain containing 2	5
51063	CALHM2	calcium homeostasis modulator 2	5
163882	CNST	consortin, connexin sorting protein	5
254531	LPCAT4	lysophosphatidylcholine acyltransferase 4	5
90273	CEACAM21	carcinoembryonic antigen related cell adhesion molecule 21	5

84142	FAM175A	family with sequence similarity 175 member A	5
23102	TBC1D2B	TBC1 domain family member 2B	5
50717	DCAF8	DDB1 and CUL4 associated factor 8	5
84447	SYVN1	synoviolin 1	5
84897	TBRG1	transforming growth factor beta regulator 1	5
9451	EIF2AK3	eukaryotic translation initiation factor 2 alpha kinase 3	5
8621	CDK13	cyclin dependent kinase 13	5
155435	RBM33	RNA binding motif protein 33	5
359845	RFLNB	refilin B	5
8535	CBX4	chromobox 4	5
79037	PVRIG	poliovirus receptor related immunoglobulin domain containing	5
80169	CTC1	CTS telomere maintenance complex component 1	5
3678	ITGA5	integrin subunit alpha 5	5
256987	SERINC5	serine incorporator 5	5
54462	CCSER2	coiled-coil serine rich protein 2	5
8527	DGKD	diacylglycerol kinase delta	5
9149	DYRK1B	dual specificity tyrosine phosphorylation regulated kinase 1B	5
246744	STH	saitohin	5
162515	SLC16A11	solute carrier family 16 member 11	5
348378	FAM159A	family with sequence similarity 159 member A	5
92840	REEP6	receptor accessory protein 6	5
8665	EIF3F	eukaryotic translation initiation factor 3 subunit F	5
393	ARHGAP4	Rho GTPase activating protein 4	5
84836	ABHD14B	abhydrolase domain containing 14B	5
9788	MTSS1	MTSS1, I-BAR domain containing	5
113878	DTX2	deltex E3 ubiquitin ligase 2	5
51092	SIDT2	SID1 transmembrane family member 2	5
23295	MGRN1	mahogunin ring finger 1	5
401944	LDLRAD2	low density lipoprotein receptor class A domain containing 2	5
11322	TMC6	transmembrane channel like 6	5
168620	BHLHA15	basic helix-loop-helix family member a15	5
84270	CARD19	caspase recruitment domain family member 19	5
151176	ERFE	erythroferrone	5
84266	ALKBH7	alkB homolog 7	5
7508	XPC	XPC complex subunit, DNA damage recognition and repair factor	5
199746	U2AF1L4	U2 small nuclear RNA auxiliary factor 1 like 4	5
10043	TOM1	target of myb1 membrane trafficking protein	5
4696	NDUFA3	NADH:ubiquinone oxidoreductase subunit A3	5
9498	SLC4A8	solute carrier family 4 member 8	5
3611	ILK	integrin linked kinase	5
6160	RPL31	ribosomal protein L31	5
283450	HECTD4	HECT domain E3 ubiquitin protein ligase 4	5
105371397	LOC105371397	uncharacterized LOC105371397	5
197358	NLRC3	NLR family CARD domain containing 3	5
6122	RPL3	ribosomal protein L3	5
30815	ST6GALNAC6	ST6 N-acetylgalactosaminide alpha-2,6-sialyltransferase 6	5
9022	CLIC3	chloride intracellular channel 3	5
56260	C8orf44	chromosome 8 open reading frame 44	5
5663	PSEN1	presenilin 1	5
23177	CEP68	centrosomal protein 68	5
9397	NMT2	N-myristoyltransferase 2	5
10868	USP20	ubiquitin specific peptidase 20	5
1107	CHD3	chromodomain helicase DNA binding protein 3	5
26112	CCDC69	coiled-coil domain containing 69	5
115992	RNF166	ring finger protein 166	5
51393	TRPV2	transient receptor potential cation channel subfamily V member 2	5
55229	PANK4	pantothenate kinase 4	5
113791	PIK3IP1	phosphoinositide-3-kinase interacting protein 1	5
92017	SNX29	sorting nexin 29	5
80095	ZNF606	zinc finger protein 606	5
51646	YPEL5	yippee like 5	5
3476	IGBP1	immunoglobulin (CD79A) binding protein 1	5
22997	IGSF9B	immunoglobulin superfamily member 9B	5
5790	PTPRCAP	protein tyrosine phosphatase, receptor type C associated protein	5
951	CD37	CD37 molecule	5

22861	NLRP1	NLR family pyrin domain containing 1	5
170622	COMMD6	COMM domain containing 6	5
2124	EVI2B	ecotropic viral integration site 2B	5
10346	TRIM22	tripartite motif containing 22	5
151556	GPR155	G protein-coupled receptor 155	5
50515	CHST11	carbohydrate sulfotransferase 11	5
472	ATM	ATM serine/threonine kinase	5
7626	ZNF75D	zinc finger protein 75D	5
7294	TXK	TXK tyrosine kinase	5
10957	PNRC1	proline rich nuclear receptor coactivator 1	5
339210	C17orf67	chromosome 17 open reading frame 67	5
51466	EVL	Enah/Vasp-like	5
9750	FAM65B	family with sequence similarity 65 member B	5
5140	PDE3B	phosphodiesterase 3B	5
4300	MLLT3	MLLT3, super elongation complex subunit	5
5252	PHF1	PHD finger protein 1	5
5330	PLCB2	phospholipase C beta 2	5
4118	MAL	mal, T-cell differentiation protein	5
63940	GPSM3	G-protein signaling modulator 3	5
645432	ARRDC5	arrestin domain containing 5	5
3932	LCK	LCK proto-oncogene, Src family tyrosine kinase	5
255394	TCP11L2	t-complex 11 like 2	5
80853	KDM7A	lysine demethylase 7A	5
140688	NOL4L	nucleolar protein 4 like	5
55643	BTBD2	BTB domain containing 2	5
6277	S100A6	S100 calcium binding protein A6	5
5800	PTPRO	protein tyrosine phosphatase, receptor type O	5
126375	ZNF792	zinc finger protein 792	5
64761	PARP12	poly(ADP-ribose) polymerase family member 12	5
51614	ERGIC3	ERGIC and golgi 3	5
90592	ZNF700	zinc finger protein 700	5
66008	TRAK2	trafficking kinesin protein 2	5
64332	NFKBIZ	NFKB inhibitor zeta	5
9710	KIAA0355	KIAA0355	5
54665	RSBN1	round spermatid basic protein 1	5
9382	COG1	component of oligomeric golgi complex 1	5
22839	DLGAP4	DLG associated protein 4	5
11035	RIPK3	receptor interacting serine/threonine kinase 3	5
57639	CCDC146	coiled-coil domain containing 146	5
23152	CIC	capicua transcriptional repressor	5
113177	IZUMO4	IZUMO family member 4	5
55568	GALNT10	polypeptide N-acetylgalactosaminyltransferase 10	5
84101	USP44	ubiquitin specific peptidase 44	5
85378	TUBGCP6	tubulin gamma complex associated protein 6	5
10673	TNFSF13B	tumor necrosis factor superfamily member 13b	5
54674	LRRN3	leucine rich repeat neuronal 3	5
6282	S100A11	S100 calcium binding protein A11	5
53827	FXYD5	FXYD domain containing ion transport regulator 5	5
79864	C11orf63	chromosome 11 open reading frame 63	5
57060	PCBP4	poly(rC) binding protein 4	5
3566	IL4R	interleukin 4 receptor	5
50650	ARHGEF3	Rho guanine nucleotide exchange factor 3	5
64393	ZMAT3	zinc finger matrin-type 3	5
5147	PDE6D	phosphodiesterase 6D	5
491	ATP2B2	ATPase plasma membrane Ca2+ transporting 2	5
129293	TRABD2A	TraB domain containing 2A	5
284802	FRG1BP	FSHD region gene 1 family member B, pseudogene	5
3702	ITK	IL2 inducible T-cell kinase	5
23253	ANKRD12	ankyrin repeat domain 12	5
5788	PTPRC	protein tyrosine phosphatase, receptor type C	5
23471	TRAM1	translocation associated membrane protein 1	5
84910	TMEM87B	transmembrane protein 87B	5
50848	F11R	F11 receptor	5
4154	MBNL1	muscleblind like splicing regulator 1	5
9595	CYTIP	cytohesin 1 interacting protein	5

57591	MKL1	megakaryoblastic leukemia (translocation) 1	5
1386	ATF2	activating transcription factor 2	5
5324	PLAG1	PLAG1 zinc finger	5
9781	RNF144A	ring finger protein 144A	5
284058	KANSL1	KAT8 regulatory NSL complex subunit 1	5
9663	LPIN2	lipin 2	5
23522	KAT6B	lysine acetyltransferase 6B	5
814	CAMK4	calcium/calmodulin dependent protein kinase IV	5
406	ARNTL	aryl hydrocarbon receptor nuclear translocator like	5
143686	SESN3	sestrin 3	5
10225	CD96	CD96 molecule	5
9262	STK17B	serine/threonine kinase 17b	5
6206	RPS12	ribosomal protein S12	5
3937	LCP2	lymphocyte cytosolic protein 2	5
8031	NCOA4	nuclear receptor coactivator 4	5
10142	AKAP9	A-kinase anchoring protein 9	5
22848	AAK1	AP2 associated kinase 1	5
129607	CMPK2	cytidine/uridine monophosphate kinase 2	5
113612	CYP2U1	cytochrome P450 family 2 subfamily U member 1	5
1508	CTSB	cathepsin B	5
18	ABAT	4-aminobutyrate aminotransferase	5
391191	OR2AK2	olfactory receptor family 2 subfamily AK member 2	5
55664	CDC37L1	cell division cycle 37 like 1	5
5334	PLCL1	phospholipase C like 1	5
6940	ZNF354A	zinc finger protein 354A	5
116986	AGAP2	ArfGAP with GTPase domain, ankyrin repeat and PH domain 2	5
3588	IL10RB	interleukin 10 receptor subunit beta	5
23064	SETX	senataxin	5
2771	GNAI2	G protein subunit alpha i2	5
26054	SENP6	SUMO1/sentrin specific peptidase 6	5
408	ARRB1	arrestin beta 1	5
9770	RASSF2	Ras association domain family member 2	5
54832	VPS13C	vacuolar protein sorting 13 homolog C	5
149951	COMMD7	COMM domain containing 7	5
54469	ZFAND6	zinc finger AN1-type containing 6	5
7188	TRAF5	TNF receptor associated factor 5	5
399	RHOH	ras homolog family member H	5
60313	GPBP1L1	GC-rich promoter binding protein 1 like 1	5
4478	MSN	moesin	5
91543	RSAD2	radical S-adenosyl methionine domain containing 2	5
115362	GBP5	guanylate binding protein 5	5
29761	USP25	ubiquitin specific peptidase 25	5
399665	FAM102A	family with sequence similarity 102 member A	5
80709	AKNA	AT-hook transcription factor	5
3603	IL16	interleukin 16	5
64098	PARVG	parvin gamma	5
64839	FBXL17	F-box and leucine rich repeat protein 17	5
9263	STK17A	serine/threonine kinase 17a	5
51176	LEF1	lymphoid enhancer binding factor 1	5
9641	IKBKE	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase epsilon	5
27250	PDCD4	programmed cell death 4 (neoplastic transformation inhibitor)	5
9402	GRAP2	GRB2-related adaptor protein 2	5
197131	UBR1	ubiquitin protein ligase E3 component n-recognin 1	5
26137	ZBTB20	zinc finger and BTB domain containing 20	5
51201	ZDHHC2	zinc finger DHHC-type containing 2	5
23112	TNRC6B	trinucleotide repeat containing 6B	5
11046	SLC35D2	solute carrier family 35 member D2	5
9665	KIAA0430	KIAA0430	5
151050	KANSL1L	KAT8 regulatory NSL complex subunit 1 like	5
7805	LAPTM5	lysosomal protein transmembrane 5	5
115294	PCMTD1	protein-L-isoaspartate (D-aspartate) O-methyltransferase domain containing 1	5
10443	N4BP2L2	NEDD4 binding protein 2 like 2	5
89846	FGD3	FYVE, RhoGEF and PH domain containing 3	5
822	CAPG	capping actin protein, gelsolin like	5
83605	CCM2	CCM2 scaffolding protein	5

83719	YPEL3	yippee like 3	5
157697	ERICH1	glutamate rich 1	5
79090	TRAPPC6A	trafficking protein particle complex 6A	5
60682	SMAP1	small ArfGAP 1	5
57561	ARRDC3	arrestin domain containing 3	5
23348	DOCK9	dedicator of cytokinesis 9	5
6904	TBCD	tubulin folding cofactor D	5
375056	MIA3	MIA family member 3, ER export factor	5
9877	ZC3H11A	zinc finger CCCH-type containing 11A	5
10608	MXD4	MAX dimerization protein 4	5
112936	VPS26B	VPS26, retromer complex component B	5
92241	RCSD1	RCSD domain containing 1	5
6709	SPTAN1	spectrin alpha, non-erythrocytic 1	5
643866	CBLN3	cerebellin 3 precursor	5
9857	CEP350	centrosomal protein 350	5
57134	MAN1C1	mannosidase alpha class 1C member 1	5
81688	C6orf62	chromosome 6 open reading frame 62	5
9459	ARHGEF6	Rac/Cdc42 guanine nucleotide exchange factor 6	5
2113	ETS1	ETS proto-oncogene 1, transcription factor	5
23118	TAB2	TGF-beta activated kinase 1/MAP3K7 binding protein 2	5
7267	TTC3	tetratricopeptide repeat domain 3	5
54014	BRWD1	bromodomain and WD repeat domain containing 1	5
157680	VPS13B	vacuolar protein sorting 13 homolog B	5
4863	NPAT	nuclear protein, coactivator of histone transcription	5
9563	H6PD	hexose-6-phosphate dehydrogenase/glucose 1-dehydrogenase	5
4650	MYO9B	myosin IXB	5
6655	SOS2	SOS Ras/Rho guanine nucleotide exchange factor 2	5
7535	ZAP70	zeta chain of T cell receptor associated protein kinase 70	5
23240	KIAA0922	KIAA0922	5
57459	GATAD2B	GATA zinc finger domain containing 2B	5
311	ANXA11	annexin A11	5
54800	KLHL24	kelch like family member 24	5
114823	LENG8	leukocyte receptor cluster member 8	5
10659	CELF2	CUGBP, Elav-like family member 2	5
57551	TAOK1	TAO kinase 1	5
9815	GIT2	GIT ArfGAP 2	5
56261	GPCPD1	glycerophosphocholine phosphodiesterase 1	5
50619	DEF6	DEF6, guanine nucleotide exchange factor	5
387082	SUMO4	small ubiquitin-like modifier 4	5
170954	PPP1R18	protein phosphatase 1 regulatory subunit 18	5
23031	MAST3	microtubule associated serine/threonine kinase 3	5
7764	ZNF217	zinc finger protein 217	5
9139	CBFA2T2	CBFA2/RUNX1 translocation partner 2	5
23508	TTC9	tetratricopeptide repeat domain 9	5
64131	XYLT1	xylosyltransferase 1	5
57594	HOMEZ	homeobox and leucine zipper encoding	5
55526	DHTKD1	dehydrogenase E1 and transketolase domain containing 1	5
57506	MAVS	mitochondrial antiviral signaling protein	5
55780	ERMARD	ER membrane associated RNA degradation	5
387119	CEP85L	centrosomal protein 85 like	5
57492	ARID1B	AT-rich interaction domain 1B	5
84726	PRRC2B	proline rich coiled-coil 2B	5
123720	WHAMM	WAS protein homolog associated with actin, golgi membranes and microtubules	5
9138	ARHGEF1	Rho guanine nucleotide exchange factor 1	5
10401	PIAS3	protein inhibitor of activated STAT 3	5
57038	RARS2	arginyl-tRNA synthetase 2, mitochondrial	5
283219	KCTD21	potassium channel tetramerization domain containing 21	5
103910	MYL12B	myosin light chain 12B	5
51084	CRYL1	crystallin lambda 1	5
79982	DNAJB14	DnaJ heat shock protein family (Hsp40) member B14	5
90324	CCDC97	coiled-coil domain containing 97	5
374868	ATP9B	ATPase phospholipid transporting 9B (putative)	5
80146	UXS1	UDP-glucuronate decarboxylase 1	5
138050	HGSNAT	heparan-alpha-glucosaminide N-acetyltransferase	5
54467	ANKIB1	ankyrin repeat and IBR domain containing 1	5

80232	WDR26	WD repeat domain 26	5
1785	DNM2	dynamin 2	5
9266	CYTH2	cytohesin 2	5
9870	AREL1	apoptosis resistant E3 ubiquitin protein ligase 1	5
93663	ARHGAP18	Rho GTPase activating protein 18	5
80790	CMIP	c-Maf inducing protein	5
752	FMNL1	formin like 1	5
10180	RBM6	RNA binding motif protein 6	5
23048	FNBP1	formin binding protein 1	5
374879	ZNF699	zinc finger protein 699	5
54838	WBP1L	WW domain binding protein 1-like	5
167153	PAPD4	poly(A) RNA polymerase D4, non-canonical	5
132864	CPEB2	cytoplasmic polyadenylation element binding protein 2	5
10618	TGOLN2	trans-golgi network protein 2	5
5978	REST	RE1 silencing transcription factor	5
54454	ATAD2B	ATPase family, AAA domain containing 2B	5
221322	TBC1D32	TBC1 domain family member 32	5
107987150			5
55716	LMBR1L	limb development membrane protein 1 like	5
5291	PIK3CB	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit beta	5
55763	EXOC1	exocyst complex component 1	5
83989	FAM172A	family with sequence similarity 172 member A	5
23181	DIP2A	disco interacting protein 2 homolog A	5
197135	PATL2	PAT1 homolog 2	5
9813	EFCAB14	EF-hand calcium binding domain 14	5
55073	LRRC37A4P	leucine rich repeat containing 37 member A4, pseudogene	5
83752	LONP2	lon peptidase 2, peroxisomal	5
84181	CHD6	chromodomain helicase DNA binding protein 6	5
29072	SETD2	SET domain containing 2	5
8850	KAT2B	lysine acetyltransferase 2B	5
11176	BAZ2A	bromodomain adjacent to zinc finger domain 2A	5
27436	EML4	echinoderm microtubule associated protein like 4	5
64224	HERPUD2	HERPUD family member 2	5
84678	KDM2B	lysine demethylase 2B	5
91749	MFSD4B	major facilitator superfamily domain containing 4B	5
9439	MED23	mediator complex subunit 23	5
55761	TTC17	tetratricopeptide repeat domain 17	5
7110	TMF1	TATA element modulatory factor 1	5
3683	ITGAL	integrin subunit alpha L	5
80821	DDHD1	DDHD domain containing 1	5
51742	ARID4B	AT-rich interaction domain 4B	5
94103	ORMDL3	ORMDL sphingolipid biosynthesis regulator 3	5
51161	C3orf18	chromosome 3 open reading frame 18	5
23228	PLCL2	phospholipase C like 2	5
146057	TTBK2	tau tubulin kinase 2	5
10260	DENND4A	DENN domain containing 4A	5
79979	TRMT2B	tRNA methyltransferase 2 homolog B	5
23347	SMCHD1	structural maintenance of chromosomes flexible hinge domain containing 1	5
259293	TAS2R30	taste 2 receptor member 30	5
7072	TIA1	TIA1 cytotoxic granule associated RNA binding protein	5
57474	ZNF490	zinc finger protein 490	5
79048	SECISBP2	SECIS binding protein 2	5
23081	KDM4C	lysine demethylase 4C	5
161176	SYNE3	spectrin repeat containing nuclear envelope family member 3	5
5095	PCCA	propionyl-CoA carboxylase alpha subunit	5
79618	HMBOX1	homeobox containing 1	5
9731	CEP104	centrosomal protein 104	5
50804	MYEF2	myelin expression factor 2	5
64236	PDLIM2	PDZ and LIM domain 2	5
10956	OS9	OS9, endoplasmic reticulum lectin	5
9517	SPTLC2	serine palmitoyltransferase long chain base subunit 2	5
5294	PIK3CG	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit gamma	5
55062	WIPI1	WD repeat domain, phosphoinositide interacting 1	5
64895	PAPOLG	poly(A) polymerase gamma	5
55106	SLFN12	schlafen family member 12	5

9170	LPAR2	lysophosphatidic acid receptor 2	5
85315	PAQR8	progestin and adipoQ receptor family member 8	5
222484	LNX2	ligand of numb-protein X 2	5
1739	DLG1	discs large MAGUK scaffold protein 1	5
6480	ST6GAL1	ST6 beta-galactoside alpha-2,6-sialyltransferase 1	5
9968	MED12	mediator complex subunit 12	5
54625	PARP14	poly(ADP-ribose) polymerase family member 14	5
25851	TECPR1	tectonin beta-propeller repeat containing 1	5
55008	HERC6	HECT and RLD domain containing E3 ubiquitin protein ligase family member 6	5
22828	SCAF8	SR-related CTD associated factor 8	5
5862	RAB2A	RAB2A, member RAS oncogene family	5
9525	VPS4B	vacuolar protein sorting 4 homolog B	5
115361	GBP4	guanylate binding protein 4	5
57020	C16orf62	chromosome 16 open reading frame 62	5
93349	SP140L	SP140 nuclear body protein like	5
6464	SHC1	SHC adaptor protein 1	5
55601	DDX60	DEXD/H-box helicase 60	5
22887	FOXJ3	forkhead box J3	5
5870	RAB6A	RAB6A, member RAS oncogene family	5
30061	SLC40A1	solute carrier family 40 member 1	5
201799	TMEM154	transmembrane protein 154	5
80063	ATF7IP2	activating transcription factor 7 interacting protein 2	5
149086	LINC01225	long intergenic non-protein coding RNA 1225	5
4033	LRMP	lymphoid restricted membrane protein	5
55770	EXOC2	exocyst complex component 2	5
3575	IL7R	interleukin 7 receptor	5
7494	XBP1	X-box binding protein 1	5
10320	IKZF1	IKAROS family zinc finger 1	5
51149	C5orf45	chromosome 5 open reading frame 45	5
7562	ZNF708	zinc finger protein 708	5
80012	PHC3	polyhomeotic homolog 3	5
637	BID	BH3 interacting domain death agonist	5
3059	HCLS1	hematopoietic cell-specific Lyn substrate 1	5
80008	TMEM156	transmembrane protein 156	5
79893	GGNBP2	gametogenetin binding protein 2	5
11016	ATF7	activating transcription factor 7	5
80167	ABHD18	abhydrolase domain containing 18	5
1385	CREB1	cAMP responsive element binding protein 1	5
64864	RFX7	regulatory factor X7	5
114908	TMEM123	transmembrane protein 123	5
56990	CDC42SE2	CDC42 small effector 2	5
84923	FAM104A	family with sequence similarity 104 member A	5
10097	ACTR2	ARP2 actin related protein 2 homolog	5
223082	ZNRF2	zinc and ring finger 2	5
80705	TSGA10	testis specific 10	5
79970	ZNF767P	zinc finger family member 767, pseudogene	5
22882	ZHX2	zinc fingers and homeoboxes 2	5
83548	COG3	component of oligomeric golgi complex 3	5
4891	SLC11A2	solute carrier family 11 member 2	5
56650	CLDND1	claudin domain containing 1	5
9235	IL32	interleukin 32	5
23533	PIK3R5	phosphoinositide-3-kinase regulatory subunit 5	5
8674	VAMP4	vesicle associated membrane protein 4	5
55303	GIMAP4	GTPase, IMAP family member 4	5
3676	ITGA4	integrin subunit alpha 4	5
1048	CEACAM5	carcinoembryonic antigen related cell adhesion molecule 5	5
6251	RSU1	Ras suppressor protein 1	5
596	BCL2	BCL2, apoptosis regulator	5
137872	ADHFE1	alcohol dehydrogenase, iron containing 1	5
120	ADD3	adducin 3	5
7454	WAS	Wiskott-Aldrich syndrome	5
283537	SLC46A3	solute carrier family 46 member 3	5
79830	ZMYM1	zinc finger MYM-type containing 1	5
81558	FAM117A	family with sequence similarity 117 member A	5
22890	ZBTB1	zinc finger and BTB domain containing 1	5

122773	KLHDC1	kelch domain containing 1	5
54893	MTMR10	myotubularin related protein 10	5
10068	IL18BP	interleukin 18 binding protein	5
90634	N4BP2L1	NEDD4 binding protein 2 like 1	5
50618	ITSN2	intersectin 2	5
1060	CENPC	centromere protein C	5
130872	AHSA2	AHA1, activator of heat shock 90kDa protein ATPase homolog 2 (yeast)	5
146691	TOM1L2	target of myb1 like 2 membrane trafficking protein	5
2595	GANC	glucosidase alpha, neutral C	5
116068	LYSMD3	LysM domain containing 3	5
54557	SGTB	small glutamine rich tetratricopeptide repeat containing beta	5
98	ACYP2	acylphosphatase 2	5
2946	GSTM2	glutathione S-transferase mu 2	5
9786	KIAA0586	KIAA0586	5
196441	ZFC3H1	zinc finger C3H1-type containing	5
5567	PRKACB	protein kinase cAMP-activated catalytic subunit beta	5
205717	USF3	upstream transcription factor family member 3	5
65981	CAPRIN2	caprin family member 2	5
25956	SEC31B	SEC31 homolog B, COPII coat complex component	5
401494	HACD4	3-hydroxyacyl-CoA dehydratase 4	5
25988	HINFP	histone H4 transcription factor	5
57035	RSRP1	arginine and serine rich protein 1	5
133418	EMB	embigin	5
6793	STK10	serine/threonine kinase 10	5
10905	MAN1A2	mannosidase alpha class 1A member 2	5
92822	ZNF276	zinc finger protein 276	5
9910	RABGAP1L	RAB GTPase activating protein 1 like	5
94039	ZNF101	zinc finger protein 101	5
84450	ZNF512	zinc finger protein 512	5
2734	GLG1	golgi glycoprotein 1	5
26091	HERC4	HECT and RLD domain containing E3 ubiquitin protein ligase 4	5
101928361	LOC101928361	uncharacterized LOC101928361	5
23043	TNIK	TRAF2 and NCK interacting kinase	5
147657	ZNF480	zinc finger protein 480	5
64921	CASD1	CAS1 domain containing 1	5
867	CBL	Cbl proto-oncogene	5
55904	KMT2E	lysine methyltransferase 2E	5
55680	RUFY2	RUN and FYVE domain containing 2	5
23469	PHF3	PHD finger protein 3	5
1803	DPP4	dipeptidyl peptidase 4	5
128077	LIX1L	limb and CNS expressed 1 like	5
5305	PIP4K2A	phosphatidylinositol-5-phosphate 4-kinase type 2 alpha	5
192669	AGO3	argonaute 3, RISC catalytic component	5
80055	PGAP1	post-GPI attachment to proteins 1	5
440193	CCDC88C	coiled-coil domain containing 88C	5
79956	ERMP1	endoplasmic reticulum metallopeptidase 1	5
440345	NPIPB4	nuclear pore complex interacting protein family member B4	5
23224	SYNE2	spectrin repeat containing nuclear envelope protein 2	5
11276	SYNRG	synergin gamma	5
114659	LRRC37B	leucine rich repeat containing 37B	5
225	ABCD2	ATP binding cassette subfamily D member 2	5
55823	VPS11	VPS11, CORVET/HOPS core subunit	5
55843	ARHGAP15	Rho GTPase activating protein 15	5
342371	ATXN1L	ataxin 1 like	5
55754	TMEM30A	transmembrane protein 30A	5
83464	APH1B	aph-1 homolog B, gamma-secretase subunit	5
641339	ZNF674	zinc finger protein 674	5
23360	FNBP4	formin binding protein 4	5
57186	RALGAPA2	Ral GTPase activating protein catalytic alpha subunit 2	5
410	ARSA	arylsulfatase A	5
27244	SESN1	sestrin 1	5
376940	ZC3H6	zinc finger CCCH-type containing 6	5
22869	ZNF510	zinc finger protein 510	5
9988	DMTF1	cyclin D binding myb like transcription factor 1	5
81550	TDRD3	tudor domain containing 3	5

6672	SP100	SP100 nuclear antigen	5
114803	MYSM1	Myb like, SWIRM and MPN domains 1	5
7431	VIM	vimentin	5
57577	CCDC191	coiled-coil domain containing 191	5
7318	UBA7	ubiquitin like modifier activating enzyme 7	5
254065	BRWD3	bromodomain and WD repeat domain containing 3	5
23200	ATP11B	ATPase phospholipid transporting 11B (putative)	5
55297	CCDC91	coiled-coil domain containing 91	5
64167	ERAP2	endoplasmic reticulum aminopeptidase 2	5
9759	HDAC4	histone deacetylase 4	5
100507419	MMP25-AS1	MMP25 antisense RNA 1	5
388585	HES5	hes family bHLH transcription factor 5	5
51621	KLF13	Kruppel like factor 13	5
150864	FAM117B	family with sequence similarity 117 member B	5
51316	PLAC8	placenta specific 8	5
57179	KIAA1191	KIAA1191	5
163050	ZNF564	zinc finger protein 564	5
2073	ERCC5	ERCC excision repair 5, endonuclease	5
81669	CCNL2	cyclin L2	5
5880	RAC2	ras-related C3 botulinum toxin substrate 2 (rho family, small GTP binding protein Rac2)	5
10207	PATJ	PATJ, crumbs cell polarity complex component	5
1265	CNN2	calponin 2	5
634	CEACAM1	carcinoembryonic antigen related cell adhesion molecule 1	5
10123	ARL4C	ADP ribosylation factor like GTPase 4C	5
121506	ERP27	endoplasmic reticulum protein 27	5
6451	SH3BGRL	SH3 domain binding glutamate rich protein like	5
84166	NLRC5	NLR family CARD domain containing 5	5
30011	SH3KBP1	SH3 domain containing kinase binding protein 1	5
23499	MACF1	microtubule-actin crosslinking factor 1	5
2186	BPTF	bromodomain PHD finger transcription factor	5
1997	ELF1	E74 like ETS transcription factor 1	5
6654	SOS1	SOS Ras/Rac guanine nucleotide exchange factor 1	5
107984315			5
1200	TPP1	tripeptidyl peptidase 1	5
80212	CCDC92	coiled-coil domain containing 92	5
1486	CTBS	chitobiase	5
27128	CYTH4	cytohesin 4	5
11261	CHP1	calcineurin like EF-hand protein 1	5
54518	APBB1IP	amyloid beta precursor protein binding family B member 1 interacting protein	5
1606	DGKA	diacylglycerol kinase alpha	5
153222	CREBRF	CREB3 regulatory factor	5
80024	SLC8B1	solute carrier family 8 member B1	5
2635	GBP3	guanylate binding protein 3	5
64784	CRTC3	CREB regulated transcription coactivator 3	5
79813	EHMT1	euchromatic histone lysine methyltransferase 1	5
8906	AP1G2	adaptor related protein complex 1 gamma 2 subunit	5
155006	TMEM213	transmembrane protein 213	5
442582	STAG3L2	stromal antigen 3-like 2 (pseudogene)	5
1182	CLCN3	chloride voltage-gated channel 3	5
51735	RAPGEF6	Rap guanine nucleotide exchange factor 6	5
92106	OXNAD1	oxidoreductase NAD binding domain containing 1	5
100420110	LOC100420110	SCY1 like pseudokinase 2 pseudogene	5
6164	RPL34	ribosomal protein L34	5
4354	MPP1	membrane palmitoylated protein 1	5
1487	CTBP1	C-terminal binding protein 1	5
58487	CREBZF	CREB/ATF bZIP transcription factor	5
4026	LPP	LIM domain containing preferred translocation partner in lipoma	5
26259	FBXW8	F-box and WD repeat domain containing 8	5
51773	RSF1	remodeling and spacing factor 1	5
6641	SNTB1	syntrophin beta 1	5
79161	TMEM243	transmembrane protein 243	5
5586	PKN2	protein kinase N2	5
64766	S100PBP	S100P binding protein	5
3460	IFNGR2	interferon gamma receptor 2 (interferon gamma transducer 1)	5

7273	TTN	titin	5
8835	SOCS2	suppressor of cytokine signaling 2	5
11320	MGAT4A	mannosyl (alpha-1,3-)-glycoprotein beta-1,4-N-acetylglucosaminyltransferase, isozyme A	5
54861	SNRK	SNF related kinase	5
4012	LNPEP	leucyl and cystinyl aminopeptidase	5
128611	ZNF831	zinc finger protein 831	5
7456	WIPF1	WAS/WASL interacting protein family member 1	5
9830	TRIM14	tripartite motif containing 14	5
50852	TRAT1	T cell receptor associated transmembrane adaptor 1	5
22990	PCNX1	pecanex homolog 1 (Drosophila)	5
11083	DIDO1	death inducer-obliterator 1	5
1106	CHD2	chromodomain helicase DNA binding protein 2	5
7644	ZNF91	zinc finger protein 91	5
1540	CYLD	CYLD lysine 63 deubiquitinase	5
643641	ZNF862	zinc finger protein 862	5
10106	CTDSP2	CTD small phosphatase 2	5
154881	KCTD7	potassium channel tetramerization domain containing 7	5
23164	MPRIP	myosin phosphatase Rho interacting protein	5
4299	AFF1	AF4/FMR2 family member 1	5
93611	FBXO44	F-box protein 44	5
7402	UTRN	utrophin	5
56204	FAM214A	family with sequence similarity 214 member A	5
6844	VAMP2	vesicle associated membrane protein 2	5
9960	USP3	ubiquitin specific peptidase 3	5
4297	KMT2A	lysine methyltransferase 2A	5
56829	ZC3HAV1	zinc finger CCCH-type containing, antiviral 1	5
139818	DOCK11	dedicator of cytokinesis 11	5
25777	SUN2	Sad1 and UNC84 domain containing 2	5
9744	ACAP1	ArfGAP with coiled-coil, ankyrin repeat and PH domains 1	5
23054	NCOA6	nuclear receptor coactivator 6	5
84162	KIAA1109	KIAA1109	5
23341	DNAJC16	DnaJ heat shock protein family (Hsp40) member C16	5
23324	MAN2B2	mannosidase alpha class 2B member 2	5
6711	SPTBN1	spectrin beta, non-erythrocytic 1	5
165631	PARP15	poly(ADP-ribose) polymerase family member 15	5
5786	PTPRA	protein tyrosine phosphatase, receptor type A	5
9535	GMFG	glia maturation factor gamma	5
256643	CXorf23	chromosome X open reading frame 23	5
55268	ECHDC2	enoyl-CoA hydratase domain containing 2	5
22838	RNF44	ring finger protein 44	5
55870	ASH1L	ASH1 like histone lysine methyltransferase	5
64780	MICAL1	microtubule associated monooxygenase, calponin and LIM domain containing 1	5
84460	ZMAT1	zinc finger matrin-type 1	5
200576	PIKFYVE	phosphoinositide kinase, FYVE-type zinc finger containing	5
58508	KMT2C	lysine methyltransferase 2C	5
8897	MTMR3	myotubularin related protein 3	5
2033	EP300	E1A binding protein p300	5
80351	TNKS2	tankyrase 2	5
9648	GCC2	GRIP and coiled-coil domain containing 2	5
163131	ZNF780B	zinc finger protein 780B	5
23335	WDR7	WD repeat domain 7	5
55599	RNPC3	RNA binding region (RNP1, RRM) containing 3	5
3716	JAK1	Janus kinase 1	5
493753	COA5	cytochrome c oxidase assembly factor 5	5
55824	PAG1	phosphoprotein membrane anchor with glycosphingolipid microdomains 1	5
114801	TMEM200A	transmembrane protein 200A	5
64750	SMURF2	SMAD specific E3 ubiquitin protein ligase 2	5
57337	SENP7	SUMO1/sentrin specific peptidase 7	5
831	CAST	calpastatin	5
257106	ARHGAP30	Rho GTPase activating protein 30	5
84945	ABHD13	abhydrolase domain containing 13	5
129285	PPP1R21	protein phosphatase 1 regulatory subunit 21	5
100507217	LINC01578	long intergenic non-protein coding RNA 1578	5
285025	CCDC141	coiled-coil domain containing 141	5

387680	FAM21A	family with sequence similarity 21 member A	5
85464	SSH2	slingshot protein phosphatase 2	5
59338	PLEKHA1	pleckstrin homology domain containing A1	5
963	CD53	CD53 molecule	5
57620	STIM2	stromal interaction molecule 2	5
10133	OPTN	optineurin	5
538	ATP7A	ATPase copper transporting alpha	5
23616	SH3BP1	SH3 domain binding protein 1	5
23304	UBR2	ubiquitin protein ligase E3 component n-recognin 2	5
10955	SERINC3	serine incorporator 3	5
22834	ZNF652	zinc finger protein 652	5
3635	INPP5D	inositol polyphosphate-5-phosphatase D	5
7767	ZNF224	zinc finger protein 224	5
92283	ZNF461	zinc finger protein 461	5
192670	AGO4	argonaute 4, RISC catalytic component	5
8631	SKAP1	src kinase associated phosphoprotein 1	5
94134	ARHGAP12	Rho GTPase activating protein 12	5
10520	ZNF211	zinc finger protein 211	5
64112	MOAP1	modulator of apoptosis 1	5
51599	LSR	lipolysis stimulated lipoprotein receptor	5
55743	CHFR	checkpoint with forkhead and ring finger domains	5
6302	TSPAN31	tetraspanin 31	5
64333	ARHGAP9	Rho GTPase activating protein 9	5
256380	SCML4	sex comb on midleg-like 4 (Drosophila)	5
83604	TMEM47	transmembrane protein 47	5
10157	AASS	aminoadipate-semialdehyde synthase	5
64926	RASAL3	RAS protein activator like 3	5
9473	THEMIS2	thymocyte selection associated family member 2	5
10983	CCNI	cyclin I	5
583	BBS2	Bardet-Biedl syndrome 2	5
25981	DNAH1	dynein axonemal heavy chain 1	5
285346	ZNF852	zinc finger protein 852	5
51088	KLHL5	kelch like family member 5	5
57707	TLDC1	TBC/LysM-associated domain containing 1	5
1523	CUX1	cut like homeobox 1	5
8509	NDST2	N-deacetylase and N-sulfotransferase 2	5
57446	NDRG3	NDRG family member 3	5
285464	CRIPAK	cysteine rich PAK1 inhibitor	5
7554	ZNF8	zinc finger protein 8	5
765	CA6	carbonic anhydrase 6	5
79567	FAM65A	family with sequence similarity 65 member A	5
23038	WDTC1	WD and tetratricopeptide repeats 1	5
9683	N4BP1	NEDD4 binding protein 1	5
5293	PIK3CD	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit delta	5
374403	TBC1D10C	TBC1 domain family member 10C	5
51339	DACT1	dishevelled binding antagonist of beta catenin 1	5
80305	TRABD	TraB domain containing	5
6932	TCF7	transcription factor 7 (T-cell specific, HMG-box)	5
3983	ABLIM1	actin binding LIM protein 1	5
10013	HDAC6	histone deacetylase 6	5
102723458	LOC102723458	uncharacterized LOC102723458	5
9961	MVP	major vault protein	5
23765	IL17RA	interleukin 17 receptor A	5
93129	ORAI3	ORAI calcium release-activated calcium modulator 3	5
100505549	LOC100505549	uncharacterized LOC100505549	5
5927	KDM5A	lysine demethylase 5A	5
7569	ZNF182	zinc finger protein 182	5
51147	ING4	inhibitor of growth family member 4	5
26119	LDLRAP1	low density lipoprotein receptor adaptor protein 1	5
6016	RIT1	Ras like without CAAX 1	5
9550	ATP6V1G1	ATPase H+ transporting V1 subunit G1	5
2592	GALT	galactose-1-phosphate uridylyltransferase	5
148932	MOB3C	MOB kinase activator 3C	5
10943	MSL3	male-specific lethal 3 homolog (Drosophila)	5
4752	NEK3	NIMA related kinase 3	5

338657	CCDC84	coiled-coil domain containing 84	5
84899	TMTC4	transmembrane and tetratricopeptide repeat containing 4	5
23355	VPS8	VPS8, CORVET complex subunit	5
23175	LPIN1	lipin 1	5
27334	P2RY10	purinergic receptor P2Y10	5
11067	C10orf10	chromosome 10 open reading frame 10	5
26959	HBP1	HMG-box transcription factor 1	5
168537	GIMAP7	GTPase, IMAP family member 7	5
10550	ARL6IP5	ADP ribosylation factor like GTPase 6 interacting protein 5	5
2005	ELK4	ELK4, ETS transcription factor	5
253260	RICTOR	RPTOR independent companion of MTOR complex 2	5
2533	FYB	FYN binding protein	5
1806	DPYD	dihydropyrimidine dehydrogenase	5
55249	YY1AP1	YY1 associated protein 1	5
55197	RPRD1A	regulation of nuclear pre-mRNA domain containing 1A	5
7586	ZKSCAN1	zinc finger with KRAB and SCAN domains 1	5
23086	EXPH5	exophilin 5	5
10006	ABI1	abl interactor 1	5
10241	CALCOCO2	calcium binding and coiled-coil domain 2	5
5926	ARID4A	AT-rich interaction domain 4A	5
5583	PRKCH	protein kinase C eta	5
7769	ZNF226	zinc finger protein 226	5
84223	IQCG	IQ motif containing G	5
284323	ZNF780A	zinc finger protein 780A	5
23476	BRD4	bromodomain containing 4	5
9611	NCOR1	nuclear receptor corepressor 1	5
51306	FAM13B	family with sequence similarity 13 member B	5
9802	DAZAP2	DAZ associated protein 2	5
5782	PTPN12	protein tyrosine phosphatase, non-receptor type 12	5
55876	GSDMB	gasdermin B	5
2804	GOLGB1	golgin B1	5
57658	CALCOCO1	calcium binding and coiled-coil domain 1	5
23558	WBP2	WW domain binding protein 2	5
147339	C18orf25	chromosome 18 open reading frame 25	5
79652	TMEM204	transmembrane protein 204	5
29108	PYCARD	PYD and CARD domain containing	5
23345	SYNE1	spectrin repeat containing nuclear envelope protein 1	5
79026	AHNAK	AHNAK nucleoprotein	5
57153	SLC44A2	solute carrier family 44 member 2	5
10505	SEMA4F	ssemaphorin 4F	5
6653	SORL1	sortilin related receptor 1	5
333929	SNAI3	snail family transcriptional repressor 3	5
1316	KLF6	Kruppel like factor 6	5
166	AES	amino-terminal enhancer of split	5
1043	CD52	CD52 molecule	5
55728	N4BP2	NEDD4 binding protein 2	5
10791	VAMP5	vesicle associated membrane protein 5	5
5257	PHKB	phosphorylase kinase regulatory subunit beta	5
23646	PLD3	phospholipase D family member 3	5
492311	IGIP	IgA inducing protein	5
9885	OSBPL2	oxysterol binding protein like 2	5
10938	EHD1	EH domain containing 1	5
1774	DNASE1L1	deoxyribonuclease 1 like 1	5
2647	BLOC1S1	biogenesis of lysosomal organelles complex 1 subunit 1	5
10870	HCST	hematopoietic cell signal transducer	5
203523	ZNF449	zinc finger protein 449	5
9924	PAN2	PAN2 poly(A) specific ribonuclease subunit	5
133619	PRRC1	proline rich coiled-coil 1	5
51276	ZNF571	zinc finger protein 571	5
144699	FBXL14	F-box and leucine rich repeat protein 14	5
389072	PLEKHM3	pleckstrin homology domain containing M3	5
23518	R3HDM1	R3H domain containing 1	5
23526	ARHGAP45	Rho GTPase activating protein 45	5
7011	TEP1	telomerase associated protein 1	5
54540	FAM193B	family with sequence similarity 193 member B	5

284996	RNF149	ring finger protein 149	5
11104	KATNA1	katanin catalytic subunit A1	5
28971	AAMDC	adipogenesis associated Mth938 domain containing	5
26053	AUTS2	autism susceptibility candidate 2	5
399687	MYO18A	myosin XVIIIA	5
57659	ZBTB4	zinc finger and BTB domain containing 4	5
400986	ANKRD36C	ankyrin repeat domain 36C	5
79741	CCDC7	coiled-coil domain containing 7	5
1629	DBT	dihydrolipoamide branched chain transacylase E2	5
93624	TADA2B	transcriptional adaptor 2B	5
162427	FAM134C	family with sequence similarity 134 member C	5
107984583			5
64788	LMF1	lipase maturation factor 1	5
7994	KAT6A	lysine acetyltransferase 6A	5
394	ARHGAP5	Rho GTPase activating protein 5	5
389	RHOC	ras homolog family member C	5
200186	CRTC2	CREB regulated transcription coactivator 2	5
10066	SCAMP2	secretory carrier membrane protein 2	5
9889	ZBED4	zinc finger BED-type containing 4	5
403313	PLPP6	phospholipid phosphatase 6	5
196528	ARID2	AT-rich interaction domain 2	5
51780	KDM3B	lysine demethylase 3B	5
5780	PTPN9	protein tyrosine phosphatase, non-receptor type 9	5
84498	FAM120B	family with sequence similarity 120B	5
23506	GLTSCR1L	GLTSCR1 like	5
26207	PITPNC1	phosphatidylinositol transfer protein, cytoplasmic 1	5
158358	KIAA2026	KIAA2026	5
387748	OR56B1	olfactory receptor family 56 subfamily B member 1	5
11201	POLI	DNA polymerase iota	5
10211	FLOT1	flotillin 1	5
200765	TIGD1	tigger transposable element derived 1	5
118	ADD1	adducin 1	5
284371	ZNF841	zinc finger protein 841	5
5142	PDE4B	phosphodiesterase 4B	5
55619	DOCK10	dedicator of cytokinesis 10	5
23527	ACAP2	ArfGAP with coiled-coil, ankyrin repeat and PH domains 2	5
23424	TDRD7	tudor domain containing 7	5
373	TRIM23	tripartite motif containing 23	5
338440	ANO9	anoctamin 9	5
10000	AKT3	AKT serine/threonine kinase 3	5
8569	MKNK1	MAP kinase interacting serine/threonine kinase 1	5
84159	ARID5B	AT-rich interaction domain 5B	5
26046	LTN1	listerin E3 ubiquitin protein ligase 1	5
23041	MON2	MON2 homolog, regulator of endosome-to-Golgi trafficking	5
60412	EXOC4	exocyst complex component 4	5
4287	ATXN3	ataxin 3	5
4343	MOV10	Mov10 RISC complex RNA helicase	5
79800	CARF	calcium responsive transcription factor	5
2776	GNAQ	G protein subunit alpha q	5
55167	MSL2	male-specific lethal 2 homolog (Drosophila)	5
83744	ZNF484	zinc finger protein 484	5
64145	RBSN	rabenosyn, RAB effector	5
55500	ETNK1	ethanolamine kinase 1	5
317	APAF1	apoptotic peptidase activating factor 1	5
51380	CSAD	cysteine sulfinic acid decarboxylase	5
55902	ACSS2	acyl-CoA synthetase short-chain family member 2	5
8567	MADD	MAP kinase activating death domain	5
7776	ZNF236	zinc finger protein 236	5

BIBLIOGRAPHY

Achuthan V, Perreira JM, Sowd GA, Puray-Chavez M, McDougall WM, Paulucci-Holthauzen A, Wu X, Fadel HJ, Poeschla EM, Multani AS, Hughes SH, Sarafianos SG, Brass AL, Engelman AN. Capsid-CPSF6 interaction licenses nuclear HIV-1 trafficking to sites of viral DNA integration. Cell Host & Microbe. 2018;24(3):392-404.e8.

Acuto O, Michel F. CD28-mediated co-stimulation: a quantitative support for TCR signalling. Nature Reviews. Immunology. 2003;3(12):939-51.

Adair P, Kim YC, Pratt KP, Scott DW. Avidity of human T cell receptor engineered CD4(+) T cells drives T-helper differentiation fate. Cellular Immunology. 2016;299:30-41.

Agosto LM, Gagne M, Henderson AJ. Impact of chromatin on HIV replication. Genes (Basel). 2015;6(4):957-76.

Agosto LM, Henderson AJ. CD4+ T cell subsets and pathways to HIV latency. AIDS Research and Human Retroviruses. 2018;34(9):780-9.

Agosto LM, Herring MB, Mothes W, Henderson AJ. HIV-1-infected CD4+ T cells facilitate latent infection of resting CD4+ T cells through cell-cell contact. Cell Reports. 2018;24(8):2088-100.

Agosto LM, Yu JJ, Dai J, Kaletsky R, Monie D, O'Doherty U. HIV-1 integrates into resting CD4+ T cells even at low inoculums as demonstrated with an improved assay for HIV-1 integration. Virology. 2007;368(1):60-72.

Ahmed N, Salsman VS, Kew Y, Shaffer D, Powell S, Zhang YJ, Grossman RG, Heslop HE, Gottschalk S. HER2-specific T cells target primary glioblastoma stem cells and induce regression of autologous experimental tumors. Clinical Cancer Research. 2010;16(2):474-85.

Aid M, Dupuy FP, Moysi E, Moir S, Haddad EK, Estes JD, Sekaly RP, Petrovas C, Ribeiro SP. Follicular CD4 T helper cells as a major HIV reservoir compartment: a molecular perspective. Frontiers in Immunology. 2018;9:895.

Allan SE, Passerini L, Bacchetta R, Crellin N, Dai M, Orban PC, Ziegler SF, Roncarolo MG, Levings MK. The role of 2 FOXP3 isoforms in the generation of human CD4+ Tregs. The Journal of Clinical Investigation. 2005;115(11):3276-84.

Allison KA, Sajti E, Collier JG, Gosselin D, Troutman TD, Stone EL, Hedrick SM, Glass CK. Affinity and dose of TCR engagement yield proportional enhancer and gene activity in CD4+ T cells. eLife. 2016;5:e10134.

Archin NM, Cheema M, Parker D, Wiegand A, Bosch RJ, Coffin JM, Eron J, Cohen M, Margolis DM. Antiretroviral intensification and valproic acid lack sustained effect on residual HIV-1 viremia or resting CD4+ cell infection. PloS One. 2010;5(2):e9390.

Archin NM, Eron JJ, Palmer S, Hartmann-Duff A, Martinson JA, Wiegand A, Bandarenko N, Schmitz JL, Bosch RJ, Landay AL, Coffin JM, Margolis DM. Valproic acid without intensified antiviral therapy has limited impact on persistent HIV infection of resting CD4+ T cells. AIDS. 2008;22(10):1131-5.

Archin NM, Espeseth A, Parker D, Cheema M, Hazuda D, Margolis DM. Expression of latent HIV induced by the potent HDAC inhibitor suberoylanilide hydroxamic acid. AIDS Research and Human Retroviruses. 2009;25(2):207-12.

Archin NM, Liberty AL, Kashuba AD, Choudhary SK, Kuruc JD, Crooks AM, Parker DC, Anderson EM, Kearney MF, Strain MC, Richman DD, Hudgens MG, Bosch RJ, Coffin JM, Eron JJ, Hazuda DJ, Margolis DM. Administration of vorinostat disrupts HIV-1 latency in patients on antiretroviral therapy. Nature. 2012;487(7408):482-5.

Armstrong JA, Horne R. Follicular dendritic cells and virus-like particles in AIDS-related lymphadenopathy. Lancet. 1984;2(8399):370-2.

Avalos CR, Abreu CM, Queen SE, Li M, Price S, Shirk EN, Engle EL, Forsyth E, Bullock BT, Mac Gabhann F, Wietgrefe SW, Haase AT, Zink MC, Mankowski JL, Clements JE, Gama L. Brain macrophages in Simian Immunodeficiency Virus-infected, antiretroviral-suppressed macaques: a functional latent reservoir. mBio. 2017;8(4):e01186-17.

Ayyanathan K, Lechner MS, Bell P, Maul GG, Schultz DC, Yamada Y, Tanaka K, Torigoe K, Rauscher FJ. Regulated recruitment of HP1 to a euchromatic gene induces mitotically heritable, epigenetic gene silencing: a mammalian cell culture model of gene variegation. Genes & Development. 2003;17(15):1855-69.

Banerjee C, Archin N, Michaels D, Belkina AC, Denis GV, Bradner J, Sebastiani P, Margolis DM, Montano M. BET bromodomain inhibition as a novel strategy for reactivation of HIV-1. Journal of Leukocyte Biology. 2012;92(6):1147-54.

Banos A, Agelopoulos M, Thanos D. Stochastic responses are not left to pure "chance". Cell. 2013;155(3):499-502.

Barboric M, Nissen RM, Kanazawa S, Jabrane-Ferrat N, Peterlin BM. NF-kappaB binds P-TEFb to stimulate transcriptional elongation by RNA polymerase II. Molecular Cell. 2001;8(2):327-37.

Barrangou R, Fremaux C, Deveau H, Richards M, Boyaval P, Moineau S, Romero DA, Horvath P. CRISPR provides acquired resistance against viruses in prokaryotes. Science. 2007;315(5819):1709-12.

Barré-Sinoussi F, Chermann JC, Rey F, Nugeyre MT, Chamaret S, Gruest J, Dauguet C, Axler-Blin C, Vézinet-Brun F, Rouzioux C, Rozenbaum W, Montagnier L. Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). Science. 1983;220(4599):868-71.

Bartholomeeusen K, Fujinaga K, Xiang Y, Peterlin BM. Histone deacetylase inhibitors (HDACis) that release the positive transcription elongation factor b (P-TEFb) from its inhibitory complex also activate HIV transcription. The Journal of Biological Chemistry. 2013;288(20):14400-7.

Bartholomeeusen K, Xiang Y, Fujinaga K, Peterlin BM. Bromodomain and extra-terminal (BET) bromodomain inhibition activate transcription via transient release of positive transcription elongation factor b (P-TEFb) from 7SK small nuclear ribonucleoprotein. The Journal of Biological Chemistry. 2012;287(43):36609-16.

Barton K, Hiener B, Winckelmann A, Rasmussen TA, Shao W, Byth K, Lanfear R, Solomon A, McMahon J, Harrington S, Buzon M, Lichterfeld M, Denton PW, Olesen R, Østergaard L, Tolstrup M, Lewin SR, Søgaard OS, Palmer S. Broad activation of latent HIV-1 in vivo. Nature Communications. 2016;7:12731.

Benchling. https://benchling.com. Accessed February 16, 2019.

Benjamini Y, Hochberg Y. Controlling the false discovery rate: A practical and powerful approach to multiple testing. The Journal of the Royal Statistical Society. Series B (Methodological). 1995; 57(1):289-300.

Bernhard W, Barreto K, Raithatha S, Sadowski I. An upstream YY1 binding site on the HIV-1 LTR contributes to latent infection. PloS One. 2013;8(10):e77052.

Bernhard W, Barreto K, Saunders A, Dahabieh MS, Johnson P, Sadowski I. The Suv39H1 methyltransferase inhibitor chaetocin causes induction of integrated HIV-1 without producing a T cell response. FEBS Letters. 2011;585(22):3549-54.

Berns EM, Klijn JG, van Staveren IL, Portengen H, Noordegraaf E, Foekens JA. Prevalence of amplification of the oncogenes c-myc, HER2/neu, and int-2 in one thousand human breast tumours: correlation with steroid receptors. European Journal of Cancer. 1992;28(2-3):697-700.

Bettini ML, Chou PC, Guy CS, Lee T, Vignali KM, Vignali DAA. Cutting Edge: CD3 ITAM diversity is required for optimal TCR signaling and thymocyte development. Journal of Immunology. 2017;199(5):1555-60.

Biberfeld P, Chayt KJ, Marselle LM, Biberfeld G, Gallo RC, Harper ME. HTLV-III expression in infected lymph nodes and relevance to pathogenesis of lymphadenopathy. The American Journal of Pathology. 1986;125(3):436-42.

Bilal MY, Zhang EY, Dinkel B, Hardy D, Yankee TM, Houtman JC. GADS is required for TCR-mediated calcium influx and cytokine release, but not cellular adhesion, in human T cells. Cellular Signalling. 2015;27(4):841-50.

Bisgrove DA, Mahmoudi T, Henklein P, Verdin E. Conserved P-TEFb-interacting domain of BRD4 inhibits HIV transcription. Proceedings of the National Academy of Sciences of the United States of America. 2007;104(34):13690-5.

Blazkova J, Chun TW, Belay BW, Murray D, Justement JS, Funk EK, Nelson A, Hallahan CW, Moir S, Wender PA, Fauci AS. Effect of histone deacetylase inhibitors on HIV production in latently infected, resting CD4(+) T cells from infected individuals receiving effective antiretroviral therapy. The Journal of Infectious Diseases. 2012;206(5):765-9.

Blazkova J, Trejbalova K, Gondois-Rey F, Halfon P, Philibert P, Guiguen A, Verdin E, Olive D, Van Lint C, Hejnar J, Hirsch I. CpG methylation controls reactivation of HIV from latency. PLoS Pathogens. 2009;5(8):e1000554.

Boehm D, Jeng M, Camus G, Gramatica A, Schwarzer R, Johnson JR, Hull PA, Montano M, Sakane N, Pagans S, Godin R, Deeks SG, Krogan NJ, Greene WC, Ott M. SMYD2-mediated histone methylation contributes to HIV-1 latency. Cell Host & Microbe. 2017;21(5):569-579.e6.

Boso G, Örvell C, Somia NV. The nature of the N-terminal amino acid residue of HIV-1 RNase H is critical for the stability of reverse transcriptase in viral particles. Journal of Virology. 2015;89(2):1286-97.

Bosque A, Planelles V. Induction of HIV-1 latency and reactivation in primary memory CD4+ T cells. Blood. 2009;113(1):58-65.

Bostik P, Mayne AE, Villinger F, Greenberg KP, Powell JD, Ansari AA. Relative resistance in the development of T cell anergy in CD4+ T cells from simian immunodeficiency virus disease-resistant sooty mangabeys. Journal of Immunology. 2001;166(1):506-16.

Bouchat S, Gatot JS, Kabeya K, Cardona C, Colin L, Herbein G, De Wit S, Clumeck N, Lambotte O, Rouzioux C, Rohr O, Van Lint C. Histone methyltransferase inhibitors induce HIV-1 recovery in resting CD4(+) T cells from HIV-1-infected HAART-treated patients. AIDS. 2012;26(12):1473-82.

Boyman O, Létourneau S, Krieg C, Sprent J. Homeostatic proliferation and survival of naïve and memory T cells. European Journal of Immunology. 2009;39(8):2088-94.

Brenchley JM, Hill BJ, Ambrozak DR, Price DA, Guenaga FJ, Casazza JP, Kuruppu J, Yazdani J, Migueles SA, Connors M, Roederer M, Douek DC, Koup RA. T-cell subsets that harbor human immunodeficiency virus (HIV) in vivo: implications for HIV pathogenesis. Journal of Virology. 2004;78(3):1160-8.

Brocken DJW, Tark-Dame M, Dame RT. dCas9: A versatile tool for epigenome editing. Current Issues in Molecular Biology. 2018;26:15-32.

Brocker T. Survival of mature CD4 T lymphocytes is dependent on major histocompatibility complex class II-expressing dendritic cells. The Journal of Experimental Medicine. 1997;186(8):1223-32.

Brownlie RJ, Zamoyska R. T cell receptor signalling networks: branched, diversified and bounded. Nature Reviews. Immunology. 2013;13(4):257-69.

Bruner KM, Murray AJ, Pollack RA, Soliman MG, Laskey SB, Capoferri AA, Lai J, Strain MC, Lada SM, Hoh R, Ho YC, Richman DD, Deeks SG, Siliciano JD, Siliciano RF. Defective proviruses rapidly accumulate during acute HIV-1 infection. Nature Medicine. 2016;22(9):1043-9.

Bunnell SC, Kapoor V, Trible RP, Zhang W, Samelson LE. Dynamic actin polymerization drives T cell receptor-induced spreading: a role for the signal transduction adaptor LAT. Immunity. 2001;14(3):315-29.

Burnett JC, Miller-Jensen K, Shah PS, Arkin AP, Schaffer DV. Control of stochastic gene expression by host factors at the HIV promoter. PLoS Pathogens. 2009;5(1):e1000260.

Calman AF, Busch MP, Vyas GN, McHugh TM, Stites DP, Peterlin BM. Transcription and replication of human immunodeficiency virus-1 in B lymphocytes in vitro. AIDS. 1988;2(3):185-93.

Cameron PU, Freudenthal PS, Barker JM, Gezelter S, Inaba K, Steinman RM. Dendritic cells exposed to human immunodeficiency virus type-1 transmit a vigorous cytopathic infection to CD4+ T cells. Science. 1992;257(5068):383-7.

Cary DC, Fujinaga K, Peterlin BM. Molecular mechanisms of HIV latency. The Journal of Clinical Investigation. 2016;126(2):448-54.

Casazza JP, Brenchley JM, Hill BJ, Ayana R, Ambrozak D, Roederer M, Douek DC, Betts MR, Koup RA. Autocrine production of beta-chemokines protects CMV-specific CD4 T cells from HIV infection. PLoS Pathogens. 2009;5(10):e1000646.

CDC. Estimated HIV incidence and prevalence in the United States, 2010-2015. HIV Surveillance Supplemental Report. 2018; 23(1).

CDC. *Pneumocystis* pneumonia --- Los Angeles. MMWR. 1981;30:250-2.

Chan DC, Kim PS. HIV entry and its inhibition. Cell. 1998;93(5):681-4.

Chavez L, Calvanese V, Verdin E. HIV latency is established directly and early in both resting and activated primary CD4 T cells. PLoS Pathogens. 2015;11(6):e1004955.

Chen J, Nikolaitchik O, Singh J, Wright A, Bencsics CE, Coffin JM, Ni N, Lockett S, Pathak VK, Hu WS. High efficiency of HIV-1 genomic RNA packaging and heterozygote formation revealed by single virion analysis. Proceedings of the National Academy of Sciences of the United States of America. 2009;106(32):13535-40.

Chicaybam L, Sodre AL, Curzio BA, Bonamino MH. An efficient low cost method for gene transfer to T lymphocytes. PloS One. 2013;8(3):e60298.

Chmielewski M, Hombach AA, Abken H. Of CARs and TRUCKs: chimeric antigen receptor (CAR) T cells engineered with an inducible cytokine to modulate the tumor stroma. Immunological Reviews. 2014;257(1):83-90.

Chmielewski M, Hombach A, Heuser C, Adams GP, Abken H. T cell activation by antibody-like immunoreceptors: increase in affinity of the single-chain fragment domain above threshold does not increase T cell activation against antigen-positive target cells but decreases selectivity. Journal of Immunology. 2004;173(12):7647-53.

Cho SW, Kim S, Kim JM, Kim JS. Targeted genome engineering in human cells with the Cas9 RNA-guided endonuclease. Nature Biotechnology. 2013;31(3):230-2.

Chomont N, El-Far M, Ancuta P, Trautmann L, Procopio FA, Yassine-Diab B, Boucher G, Boulassel MR, Ghattas G, Brenchley JM, Schacker TW, Hill BJ, Douek DC, Routy JP, Haddad EK, Sékaly RP. HIV reservoir size and persistence are driven by T cell survival and homeostatic proliferation. Nature Medicine. 2009;15(8):893-900.

Chun TW, Engel D, Berrey MM, Shea T, Corey L, Fauci AS. Early establishment of a pool of latently infected, resting CD4(+) T cells during primary HIV-1 infection. Proceedings of the National Academy of Sciences of the United States of America. 1998;95(15):8869-73.

Chun TW, Stuyver L, Mizell SB, Ehler LA, Mican JA, Baseler M, Lloyd AL, Nowak MA, Fauci AS. Presence of an inducible HIV-1 latent reservoir during highly active antiretroviral therapy. Proceedings of the National Academy of Sciences of the United States of America. 1997;94(24):13193-7.

Colin L, Van Lint C. Molecular control of HIV-1 postintegration latency: implications for the development of new therapeutic strategies. Retrovirology. 2009;6:111.

Cong L, Ran FA, Cox D, Lin S, Barretto R, Habib N, Hsu PD, Wu X, Jiang W, Marraffini LA, Zhang F. Multiplex genome engineering using CRISPR/Cas systems. Science. 2013;339(6121):819-23.

Connor RI, Sheridan KE, Ceradini D, Choe S, Landau NR. Change in coreceptor use correlates with disease progression in HIV-1--infected individuals. The Journal of Experimental Medicine. 1997;185(4):621-8.

Conrad RJ, Fozouni P, Thomas S, Sy H, Zhang Q, Zhou MM, Ott M. The Short Isoform of BRD4 Promotes HIV-1 Latency by Engaging Repressive SWI/SNF Chromatin-Remodeling Complexes. Molecular Cell. 2017;67(6):1001-1012.e6.

Contreras X, Schweneker M, Chen CS, McCune JM, Deeks SG, Martin J, Peterlin BM. Suberoylanilide hydroxamic acid reactivates HIV from latently infected cells. The Journal of Biological Chemistry. 2009;284(11):6782-9.

Dahabieh MS, Ooms M, Brumme C, Taylor J, Harrigan PR, Simon V, Sadowski I. Direct non-productive HIV-1 infection in a T-cell line is driven by cellular activation state and NFκB. Retrovirology. 2014;11:17.

Dai M, Wang P, Boyd AD, Kostov G, Athey B, Jones EG, Bunney WE, Myers RM, Speed TP, Akil H, Watson SJ, Meng F. Evolving gene/transcript definitions significantly alter the interpretation of GeneChip data. Nucleic Acids Research. 2005;33(20):e175.

Dar RD, Hosmane NN, Arkin MR, Siliciano RF, Weinberger LS. Screening for noise in gene expression identifies drug synergies. Science. 2014;344(6190):1392-6.

Darcis G, Kula A, Bouchat S, Fujinaga K, Corazza F, Ait-Ammar A, Delacourt N, Melard A, Kabeya K, Vanhulle C, Van Driessche B, Gatot JS, Cherrier T, Pianowski LF, Gama L, Schwartz C, Vila J, Burny A, Clumeck N, Moutschen M, De Wit S, Peterlin BM, Rouzioux C, Rohr O, Van Lint C. An in-depth comparison of latency-reversing agent combinations in various in vitro and ex vivo HIV-1 latency models identified Bryostatin-1+JQ1 and Ingenol-B+JQ1 to potently reactivate viral gene expression. PLoS Pathogens. 2015;11(7):e1005063.

Darcis G, Van Driessche B, Van Lint C. HIV latency: should we shock or lock. Trends in Immunology. 2017;38(3):217-28.

Davis CB, Dikic I, Unutmaz D, Hill CM, Arthos J, Siani MA, Thompson DA, Schlessinger J, Littman DR. Signal transduction due to HIV-1 envelope interactions

with chemokine receptors CXCR4 or CCR5. The Journal of Experimental Medicine. 1997;186(10):1793-8.

De Cock KM, Jaffe HW, Curran JW. The evolving epidemiology of HIV/AIDS. AIDS. 2012;26(10):1205-13.

Debyser Z, Vansant G, Bruggemans A, Janssens J, Christ F. Insight in HIV integration site selection provides a block-and-lock strategy for a functional cure of HIV infection. Viruses. 2018;11(1):E12.

Dembić Z, Haas W, Weiss S, McCubrey J, Kiefer H, von Boehmer H, Steinmetz M. Transfer of specificity by murine alpha and beta T-cell receptor genes. Nature. 1986;320(6059):232-8.

Demoustier A, Gubler B, Lambotte O, de Goër MG, Wallon C, Goujard C, Delfraissy JF, Taoufik Y. In patients on prolonged HAART, a significant pool of HIV infected CD4 T cells are HIV-specific. AIDS. 2002;16(13):1749-54.

Deng H, Liu R, Ellmeier W, Choe S, Unutmaz D, Burkhart M, Di Marzio P, Marmon S, Sutton RE, Hill CM, Davis CB, Peiper SC, Schall TJ, Littman DR, Landau NR. Identification of a major co-receptor for primary isolates of HIV-1. Nature. 1996;381(6584):661-6.

Donahue DA, Kuhl BD, Sloan RD, Wainberg MA. The viral protein Tat can inhibit the establishment of HIV-1 latency. Journal of Virology. 2012;86(6):3253-63.

Douek DC, Brenchley JM, Betts MR, Ambrozak DR, Hill BJ, Okamoto Y, Casazza JP, Kuruppu J, Kunstman K, Wolinsky S, Grossman Z, Dybul M, Oxenius A, Price DA, Connors M, Koup RA. HIV preferentially infects HIV-specific CD4+ T cells. Nature. 2002;417(6884):95-8.

Dragic T, Litwin V, Allaway GP, Martin SR, Huang Y, Nagashima KA, Cayanan C, Maddon PJ, Koup RA, Moore JP, Paxton WA. HIV-1 entry into CD4+ cells is mediated by the chemokine receptor CC-CKR-5. Nature. 1996;381(6584):667-73.

Duverger A, Jones J, May J, Bibollet-Ruche F, Wagner FA, Cron RQ, Kutsch O. Determinants of the establishment of human immunodeficiency virus type 1 latency. Journal of Virology. 2009;83(7):3078-93.

Elliott JH, Wightman F, Solomon A, Ghneim K, Ahlers J, Cameron MJ, Smith MZ, Spelman T, McMahon J, Velayudham P, Brown G, Roney J, Watson J, Prince MH, Hoy JF, Chomont N, Fromentin R, Procopio FA, Zeidan J, Palmer S, Odevall L, Johnstone RW, Martin BP, Sinclair E, Deeks SG, Hazuda DJ, Cameron PU, Sékaly RP, Lewin SR. Activation of HIV transcription with short-course vorinostat in HIV-

infected patients on suppressive antiretroviral therapy. PLoS Pathogens. 2014;10(10):e1004473.

Emery A, Zhou S, Pollom E, Swanstrom R. Characterizing HIV-1 splicing by using next-generation sequencing. Journal of Virology. 2017;91(6):e02515-16.

Emiliani S, Van Lint C, Fischle W, Paras P, Ott M, Brady J, Verdin E. A point mutation in the HIV-1 Tat responsive element is associated with postintegration latency. Proceedings of the National Academy of Sciences of the United States of America. 1996;93(13):6377-81.

Fakruddin JM, Lempicki RA, Gorelick RJ, Yang J, Adelsberger JW, Garcia-Pineres AJ, Pinto LA, Lane HC, Imamichi T. Noninfectious papilloma virus-like particles inhibit HIV-1 replication: implications for immune control of HIV-1 infection by IL-27. Blood. 2007;109(5):1841-9.

Feinberg MB, Baltimore D, Frankel AD. The role of Tat in the human immunodeficiency virus life cycle indicates a primary effect on transcriptional elongation. Proceedings of the National Academy of Sciences of the United States of America. 1991;88(9):4045-9.

Fenard D, Yonemoto W, de Noronha C, Cavrois M, Williams SA, Greene WC. Nef is physically recruited into the immunological synapse and potentiates T cell activation early after TCR engagement. Journal of Immunology. 2005;175(9):6050-7.

Feng K, Liu Y, Guo Y, Qiu J, Wu Z, Dai H, Yang Q, Wang Y, Han W. Phase I study of chimeric antigen receptor modified T cells in treating HER2-positive advanced biliary tract cancers and pancreatic cancers. Protein & Cell. 2018;9(10):838-47.

Feng Y, Broder CC, Kennedy PE, Berger EA. HIV-1 entry cofactor: functional cDNA cloning of a seven-transmembrane, G protein-coupled receptor. Science. 1996;272(5263):872-7.

Feucht J, Sun J, Eyquem J, Ho YJ, Zhao Z, Leibold J, Dobrin A, Cabriolu A, Hamieh M, Sadelain M. Calibration of CAR activation potential directs alternative T cell fates and therapeutic potency. Nature Medicine. 2019;25(1):82-8.

Finzi D, Hermankova M, Pierson T, Carruth LM, Buck C, Chaisson RE, Quinn TC, Chadwick K, Margolick J, Brookmeyer R, Gallant J, Markowitz M, Ho DD, Richman DD, Siliciano RF. Identification of a reservoir for HIV-1 in patients on highly active antiretroviral therapy. Science. 1997;278(5341):1295-300.

Fischer U, Huber J, Boelens WC, Mattaj IW, Lührmann R. The HIV-1 Rev activation domain is a nuclear export signal that accesses an export pathway used by specific cellular RNAs. Cell. 1995;82(3):475-83.

Folks TM, Clouse KA, Justement J, Rabson A, Duh E, Kehrl JH, Fauci AS. Tumor necrosis factor alpha induces expression of human immunodeficiency virus in a chronically infected T-cell clone. Proceedings of the National Academy of Sciences of the United States of America. 1989;86(7):2365-8.

Frank GA, Narayan K, Bess JW, Del Prete GQ, Wu X, Moran A, Hartnell LM, Earl LA, Lifson JD, Subramaniam S. Maturation of the HIV-1 core by a non-diffusional phase transition. Nature Communications. 2015;6:5854.

Franza BR, Rauscher FJ, Josephs SF, Curran T. The Fos complex and Fos-related antigens recognize sequence elements that contain AP-1 binding sites. Science. 1988;239(4844):1150-3.

Frazer IH, Mackay IR, Crapper RM, Jones B, Gust ID, Sarngadharan MG, Campbell DC, Ungar B. Immunological abnormalities in asymptomatic homosexual men: correlation with antibody to HTLV-III and sequential changes over two years. The Quarterly Journal of Medicine. 1986;61(234):921-33.

Frearson JA, Alexander DR. The phosphotyrosine phosphatase SHP-2 participates in a multimeric signaling complex and regulates T cell receptor (TCR) coupling to the Ras/mitogen-activated protein kinase (MAPK) pathway in Jurkat T cells. The Journal of Experimental Medicine. 1998;187(9):1417-26.

Freiberg MS, Chang CC, Kuller LH, Skanderson M, Lowy E, Kraemer KL, Butt AA, Bidwell Goetz M, Leaf D, Oursler KA, Rimland D, Rodriguez Barradas M, Brown S, Gibert C, McGinnis K, Crothers K, Sico J, Crane H, Warner A, Gottlieb S, Gottdiener J, Tracy RP, Budoff M, Watson C, Armah KA, Doebler D, Bryant K, Justice AC. HIV infection and the risk of acute myocardial infarction. JAMA Internal Medicine. 2013;173(8):614-22.

French MA, King MS, Tschampa JM, da Silva BA, Landay AL. Serum immune activation markers are persistently increased in patients with HIV infection after 6 years of antiretroviral therapy despite suppression of viral replication and reconstitution of CD4+ T cells. The Journal of Infectious Diseases. 2009;200(8):1212-5.

Friedman J, Cho WK, Chu CK, Keedy KS, Archin NM, Margolis DM, Karn J. Epigenetic silencing of HIV-1 by the histone H3 lysine 27 methyltransferase enhancer of Zeste 2. Journal of Virology. 2011;85(17):9078-89.

Friedman JR, Fredericks WJ, Jensen DE, Speicher DW, Huang XP, Neilson EG, Rauscher FJ. KAP-1, a novel corepressor for the highly conserved KRAB repression domain. Genes & Development. 1996;10(16):2067-78.

Fu Y, Foden JA, Khayter C, Maeder ML, Reyon D, Joung JK, Sander JD. High-frequency off-target mutagenesis induced by CRISPR-Cas nucleases in human cells. Nature Biotechnology. 2013;31(9):822-6.

Fujinaga K, Irwin D, Huang Y, Taube R, Kurosu T, Peterlin BM. Dynamics of human immunodeficiency virus transcription: P-TEFb phosphorylates RD and dissociates negative effectors from the transactivation response element. Molecular and Cellular Biology. 2004;24(2):787-95.

Fujinaga K, Luo Z, Schaufele F, Peterlin BM. Visualization of positive transcription elongation factor b (P-TEFb) activation in living cells. The Journal of Biological Chemistry. 2015;290(3):1829-36.

Gagne M, Michaels D, Schiralli Lester G, Wong W, Gummuluru S, Henderson AJ. Strength of T cell signaling regulates HIV-1 replication and establishment of latency. bioRxiv. https://doi.org/10.1101/432401.

Gallo RC, Montagnier L. The discovery of HIV as the cause of AIDS. The New England Journal of Medicine. 2003;349(24):2283-5.

Gao F, Bailes E, Robertson DL, Chen Y, Rodenburg CM, Michael SF, Cummins LB, Arthur LO, Peeters M, Shaw GM, Sharp PM, Hahn BH. Origin of HIV-1 in the chimpanzee Pan troglodytes troglodytes. Nature. 1999;397(6718):436-41.

Garcia JA, Wu FK, Mitsuyasu R, Gaynor RB. Interactions of cellular proteins involved in the transcriptional regulation of the human immunodeficiency virus. The EMBO Journal. 1987;6(12):3761-70.

Garriga J, Peng J, Parreño M, Price DH, Henderson EE, Graña X. Upregulation of cyclin T1/CDK9 complexes during T cell activation. Oncogene. 1998;17(24):3093-102.

Gautier L, Cope L, Bolstad BM, Irizarry RA. affy--analysis of Affymetrix GeneChip data at the probe level. Bioinformatics. 2004;20(3):307-15.

Geldmacher C, Ngwenyama N, Schuetz A, Petrovas C, Reither K, Heeregrave EJ, Casazza JP, Ambrozak DR, Louder M, Ampofo W, Pollakis G, Hill B, Sanga E, Saathoff E, Maboko L, Roederer M, Paxton WA, Hoelscher M, Koup RA. Preferential infection and depletion of Mycobacterium tuberculosis-specific CD4 T cells after HIV-1 infection. The Journal of Experimental Medicine. 2010;207(13):2869-81.

Gentleman RC, Carey VJ, Bates DM, Bolstad B, Dettling M, Dudoit S, Ellis B, Gautier L, Ge Y, Gentry J, Hornik K, Hothorn T, Huber W, Iacus S, Irizarry R, Leisch F, Li C, Maechler M, Rossini AJ, Sawitzki G, Smith C, Smyth G, Tierney L, Yang JY,

Zhang J. Bioconductor: open software development for computational biology and bioinformatics. Genome Biology. 2004;5(10):R80.

Gibson S, August A, Branch D, Dupont B, Mills GM. Functional LCK Is required for optimal CD28-mediated activation of the TEC family tyrosine kinase EMT/ITK. The Journal of Biological Chemistry. 1996;271(12):7079-83.

Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, Goicochea P, Casapía M, Guanira-Carranza JV, Ramirez-Cardich ME, Montoya-Herrera O, Fernández T, Veloso VG, Buchbinder SP, Chariyalertsak S, Schechter M, Bekker LG, Mayer KH, Kallás EG, Amico KR, Mulligan K, Bushman LR, Hance RJ, Ganoza C, Defechereux P, Postle B, Wang F, McConnell JJ, Zheng JH, Lee J, Rooney JF, Jaffe HS, Martinez AI, Burns DN, Glidden DV, iPrEx Study Team. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. The New England Journal of Medicine. 2010;363(27):2587-99.

Gray GE, Allen M, Moodie Z, Churchyard G, Bekker LG, Nchabeleng M, Mlisana K, Metch B, de Bruyn G, Latka MH, Roux S, Mathebula M, Naicker N, Ducar C, Carter DK, Puren A, Eaton N, McElrath MJ, Robertson M, Corey L, Kublin JG, Alexander S, Corey L, Ducar C, Duerr A, Eaton N, McElrath J, Holt R, Hural J, Kublin J, Wecker M, Escamilla G, Holman D, Metch B, Moodie Z, Self S, Allen M, Fix A, Follman D, Johnston P, Luzar MA, Martinez A, Casimiro D, Isaacs R, Kierstead L, Leavitt R, Mehrotra D, Robertson M, DeBruyn G, Gray G, Nkala B, Magopane T, Mkhise B, Lehobye I, Mathebula MP, Nchabeleng M, Bekker LG, Ronan A, Roux S, Churchyard G, Latka M, Lion-Cachet C, Mngadi K, Nielson T, Selepe P, Bennie T, Mlisana K, Naicker N, Puren A, Galetta D, Levendal E. Safety and efficacy of the HVTN 503/Phambili study of a clade-B-based HIV-1 vaccine in South Africa: a double-blind, randomised, placebo-controlled test-of-concept phase 2b study. The Lancet. Infectious Diseases. 2011;11(7):507-15.

Groner AC, Meylan S, Ciuffi A, Zangger N, Ambrosini G, Dénervaud N, Bucher P, Trono D. KRAB-zinc finger proteins and KAP1 can mediate long-range transcriptional repression through heterochromatin spreading. PLoS Genetics. 2010;6(3):e1000869.

Gross G, Eshhar Z. Endowing T cells with antibody specificity using chimeric T cell receptors. Federation of American Societies for Experimental Biology Journal. 1992;6(15):3370-8.

Gruters RA, Otto SA, Al BJ, Verhoeven AJ, Verweij CL, Van Lier RA, Miedema F. Non-mitogenic T cell activation signals are sufficient for induction of human immunodeficiency virus transcription. European Journal of Immunology. 1991;21(1):167-72.

Guaraldi G, Orlando G, Zona S, Menozzi M, Carli F, Garlassi E, Berti A, Rossi E, Roverato A, Palella F. Premature age-related comorbidities among HIV-infected persons compared with the general population. Clinical Infectious Diseases. 2011;53(11):1120-6.

Güerri-Fernández R, Molina-Morant D, Villar-García J, Herrera S, González-Mena A, Guelar A, Trenchs-Rodríguez M, Díez-Pérez A, Knobel H. Bone density, microarchitecture, and tissue quality after long-term treatment with Tenofovir/Emtricitabine or Abacavir/Lamivudine. Journal of Acquired Immune Deficiency Syndromes. 2017;75(3):322-7.

Hamer DH. Can HIV be Cured? Mechanisms of HIV persistence and strategies to combat it. Current HIV Research. 2004;2(2):99-111.

Han Y, Lassen K, Monie D, Sedaghat AR, Shimoji S, Liu X, Pierson TC, Margolick JB, Siliciano RF, Siliciano JD. Resting CD4+ T cells from human immunodeficiency virus type 1 (HIV-1)-infected individuals carry integrated HIV-1 genomes within actively transcribed host genes. Journal of Virology. 2004;78(12):6122-33.

Harrigan PR, Whaley M, Montaner JS. Rate of HIV-1 RNA rebound upon stopping antiretroviral therapy. AIDS. 1999;13(8):F59-62.

Hatano H, Jain V, Hunt PW, Lee TH, Sinclair E, Do TD, Hoh R, Martin JN, McCune JM, Hecht F, Busch MP, Deeks SG. Cell-based measures of viral persistence are associated with immune activation and programmed cell death protein 1 (PD-1)-expressing CD4+ T cells. The Journal of Infectious Diseases. 2013;208(1):50-6.

Hauber J, Cullen BR. Mutational analysis of the trans-activation-responsive region of the human immunodeficiency virus type I long terminal repeat. Journal of Virology. 1988;62(3):673-9.

He G, Margolis DM. Counterregulation of chromatin deacetylation and histone deacetylase occupancy at the integrated promoter of human immunodeficiency virus type 1 (HIV-1) by the HIV-1 repressor YY1 and HIV-1 activator Tat. Molecular and Cellular Biology. 2002;22(9):2965-73.

Hegedus A, Kavanagh Williamson M, Huthoff H. HIV-1 pathogenicity and virion production are dependent on the metabolic phenotype of activated CD4+ T cells. Retrovirology. 2014;11:98.

Hladik F, Sakchalathorn P, Ballweber L, Lentz G, Fialkow M, Eschenbach D, McElrath MJ. Initial events in establishing vaginal entry and infection by human immunodeficiency virus type-1. Immunity. 2007;26(2):257-70.

Ho YC, Shan L, Hosmane NN, Wang J, Laskey SB, Rosenbloom DI, Lai J, Blankson JN, Siliciano JD, Siliciano RF. Replication-competent noninduced proviruses in the latent reservoir increase barrier to HIV-1 cure. Cell. 2013;155(3):540-51.

Hollenbaugh JA, Munger J, Kim B. Metabolite profiles of human immunodeficiency virus infected CD4+ T cells and macrophages using LC-MS/MS analysis. Virology. 2011;415(2):153-9.

Honeycutt JB, Thayer WO, Baker CE, Ribeiro RM, Lada SM, Cao Y, Cleary RA, Hudgens MG, Richman DD, Garcia JV. HIV persistence in tissue macrophages of humanized myeloid-only mice during antiretroviral therapy. Nature Medicine. 2017;23(5):638-43.

Hosmane NN, Kwon KJ, Bruner KM, Capoferri AA, Beg S, Rosenbloom DI, Keele BF, Ho YC, Siliciano JD, Siliciano RF. Proliferation of latently infected CD4+ T cells carrying replication-competent HIV-1: Potential role in latent reservoir dynamics. The Journal of Experimental Medicine. 2017;214(4):959-72.

Hu H, Liu F, Kim J, Ratto-Kim S. HIV Susceptibility of human antigen-specific CD4 T cells in AIDS pathogenesis and vaccine response. Expert Review of Vaccines. 2016;15(6):709-17.

Hu W, Kaminski R, Yang F, Zhang Y, Cosentino L, Li F, Luo B, Alvarez-Carbonell D, Garcia-Mesa Y, Karn J, Mo X, Khalili K. RNA-directed gene editing specifically eradicates latent and prevents new HIV-1 infection. Proceedings of the National Academy of Sciences of the United States of America. 2014;111(31):11461-6.

Huang LM, Joshi A, Willey R, Orenstein J, Jeang KT. Human immunodeficiency viruses regulated by alternative trans-activators: genetic evidence for a novel non-transcriptional function of Tat in virion infectivity. The EMBO Journal. 1994;13(12):2886-96.

Huang Y, Wange RL. T cell receptor signaling: beyond complex complexes. The Journal of Biological Chemistry. 2004;279(28):28827-30.

Hunt PW, Martin JN, Sinclair E, Bredt B, Hagos E, Lampiris H, Deeks SG. T cell activation is associated with lower CD4+ T cell gains in human immunodeficiency virus-infected patients with sustained viral suppression during antiretroviral therapy. The Journal of Infectious Diseases. 2003;187(10):1534-43.

Imlach S, Leen C, Bell JE, Simmonds P. Phenotypic analysis of peripheral blood gammadelta T lymphocytes and their targeting by human immunodeficiency virus type 1 in vivo. Virology. 2003;305(2):415-27.

Irizarry RA, Hobbs B, Collin F, Beazer-Barclay YD, Antonellis KJ, Scherf U, Speed TP. Exploration, normalization, and summaries of high density oligonucleotide array probe level data. Biostatistics. 2003;4(2):249-64.

Ivanov AV, Peng H, Yurchenko V, Yap KL, Negorev DG, Schultz DC, Psulkowski E, Fredericks WJ, White DE, Maul GG, Sadofsky MJ, Zhou MM, Rauscher FJ. PHD domain-mediated E3 ligase activity directs intramolecular sumoylation of an adjacent bromodomain required for gene silencing. Molecular Cell. 2007;28(5):823-37.

Jacobs FM, Greenberg D, Nguyen N, Haeussler M, Ewing AD, Katzman S, Paten B, Salama SR, Haussler D. An evolutionary arms race between KRAB zinc-finger genes ZNF91/93 and SVA/L1 retrotransposons. Nature. 2014;516(7530):242-5.

Jadlowsky JK, Wong JY, Graham AC, Dobrowolski C, Devor RL, Adams MD, Fujinaga K, Karn J. Negative elongation factor is required for the maintenance of proviral latency but does not induce promoter-proximal pausing of RNA polymerase II on the HIV long terminal repeat. Molecular and Cellular Biology. 2014;34(11):1911-28.

Janas AM, Wu L. HIV-1 interactions with cells: from viral binding to cell-cell transmission. Current Protocols in Cell Biology. 2009;Chapter 26:Unit 26.5.

Jinek M, Chylinski K, Fonfara I, Hauer M, Doudna JA, Charpentier E. A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity. Science. 2012;337(6096):816-21.

Jordan A, Bisgrove D, Verdin E. HIV reproducibly establishes a latent infection after acute infection of T cells in vitro. The EMBO Journal. 2003;22(8):1868-77.

Kaczmarek Michaels K, Wolschendorf F, Schiralli Lester GM, Natarajan M, Kutsch O, Henderson AJ. RNAP II processivity is a limiting step for HIV-1 transcription independent of orientation to and activity of endogenous neighboring promoters. Virology. 2015;486:7-14.

Kaminski R, Bella R, Yin C, Otte J, Ferrante P, Gendelman HE, Li H, Booze R, Gordon J, Hu W, Khalili K. Excision of HIV-1 DNA by gene editing: a proof-of-concept in vivo study. Gene Therapy. 2016;23(8-9):690-5.

Karmaus PWF, Chen X, Lim SA, Herrada AA, Nguyen TM, Xu B, Dhungana Y, Rankin S, Chen W, Rosencrance C, Yang K, Fan Y, Cheng Y, Easton J, Neale G, Vogel P, Chi H. Metabolic heterogeneity underlies reciprocal fates of T_H17 cell stemness and plasticity. Nature. 2019;565(7737):101-5.

Kauder SE, Bosque A, Lindqvist A, Planelles V, Verdin E. Epigenetic regulation of HIV-1 latency by cytosine methylation. PLoS Pathogens. 2009;5(6):e1000495.

Kessl JJ, Kutluay SB, Townsend D, Rebensburg S, Slaughter A, Larue RC, Shkriabai N, Bakouche N, Fuchs JR, Bieniasz PD, Kvaratskhelia M. HIV-1 integrase binds the viral RNA genome and is essential during virion morphogenesis. Cell. 2016;166(5):1257-1268.e12.

Kharsany AB, Karim QA. HIV infection and AIDS in sub-Saharan Africa: Current status, challenges and opportunities. The Open AIDS Journal. 2016;10:34-48.

Kim D, Bae S, Park J, Kim E, Kim S, Yu HR, Hwang J, Kim JI, Kim JS. Digenome-seq: genome-wide profiling of CRISPR-Cas9 off-target effects in human cells. Nature Methods. 2015;12(3):237-43, 1 p following 243.

Kim M, Hosmane NN, Bullen CK, Capoferri A, Yang HC, Siliciano JD, Siliciano RF. A primary CD4(+) T cell model of HIV-1 latency established after activation through the T cell receptor and subsequent return to quiescence. Nature Protocols. 2014;9(12):2755-70.

Kim YK, Mbonye U, Hokello J, Karn J. T-cell receptor signaling enhances transcriptional elongation from latent HIV proviruses by activating P-TEFb through an ERK-dependent pathway. Journal of Molecular Biology. 2011;410(5):896-916.

Klotman ME, Kim S, Buchbinder A, DeRossi A, Baltimore D, Wong-Staal F. Kinetics of expression of multiply spliced RNA in early human immunodeficiency virus type 1 infection of lymphocytes and monocytes. Proceedings of the National Academy of Sciences of the United States of America. 1991;88(11):5011-5.

Koenig S, Gendelman HE, Orenstein JM, Dal Canto MC, Pezeshkpour GH, Yungbluth M, Janotta F, Aksamit A, Martin MA, Fauci AS. Detection of AIDS virus in macrophages in brain tissue from AIDS patients with encephalopathy. Science. 1986;233(4768):1089-93.

Koh Y, Wu X, Ferris AL, Matreyek KA, Smith SJ, Lee K, KewalRamani VN, Hughes SH, Engelman A. Differential effects of human immunodeficiency virus type 1 capsid and cellular factors nucleoporin 153 and LEDGF/p75 on the efficiency and specificity of viral DNA integration. Journal of Virology. 2013;87(1):648-58.

Koup RA, Safrit JT, Cao Y, Andrews CA, McLeod G, Borkowsky W, Farthing C, Ho DD. Temporal association of cellular immune responses with the initial control of viremia in primary human immunodeficiency virus type 1 syndrome. Journal of Virology. 1994;68(7):4650-5.

Kumar NA, Cheong K, Powell DR, da Fonseca Pereira C, Anderson J, Evans VA, Lewin SR, Cameron PU. The role of antigen presenting cells in the induction of HIV-1 latency in resting CD4(+) T-cells. Retrovirology. 2015;12:76.

Kumar NA, van der Sluis RM, Mota T, Pascoe R, Evans VA, Lewin SR, Cameron PU. Myeloid dendritic cells induce HIV latency in proliferating CD4+ T cells. Journal of Immunology. 2018;201(5):1468-77.

Lassen KG, Hebbeler AM, Bhattacharyya D, Lobritz MA, Greene WC. A flexible model of HIV-1 latency permitting evaluation of many primary CD4 T-cell reservoirs. PloS One. 2012;7(1):e30176.

Laurence J, Hodtsev AS, Posnett DN. Superantigen implicated in dependence of HIV-1 replication in T cells on TCR V beta expression. Nature. 1992;358(6383):255-9.

Lawhorn IE, Ferreira JP, Wang CL. Evaluation of sgRNA target sites for CRISPR-mediated repression of TP53. PloS One. 2014;9(11):e113232.

Lee J, Dull TJ, Lax I, Schlessinger J, Ullrich A. HER2 cytoplasmic domain generates normal mitogenic and transforming signals in a chimeric receptor. The EMBO Journal. 1989;8(1):167-73.

Lehrman G, Hogue IB, Palmer S, Jennings C, Spina CA, Wiegand A, Landay AL, Coombs RW, Richman DD, Mellors JW, Coffin JM, Bosch RJ, Margolis DM. Depletion of latent HIV-1 infection in vivo: a proof-of-concept study. Lancet. 2005;366(9485):549-55.

Lelek M, Casartelli N, Pellin D, Rizzi E, Souque P, Severgnini M, Di Serio C, Fricke T, Diaz-Griffero F, Zimmer C, Charneau P, Di Nunzio F. Chromatin organization at the nuclear pore favours HIV replication. Nature Communications. 2015;6:6483.

Li Z, Guo J, Wu Y, Zhou Q. The BET bromodomain inhibitor JQ1 activates HIV latency through antagonizing Brd4 inhibition of Tat-transactivation. Nucleic Acids Research. 2013;41(1):277-87.

Lillemeier BF, Mörtelmaier MA, Forstner MB, Huppa JB, Groves JT, Davis MM. TCR and Lat are expressed on separate protein islands on T cell membranes and concatenate during activation. Nature Immunology. 2010;11(1):90-6.

Llewellyn GN, Alvarez-Carbonell D, Chateau M, Karn J, Cannon PM. HIV-1 infection of microglial cells in a reconstituted humanized mouse model and identification of compounds that selectively reverse HIV latency. Journal of Neurovirology. 2018;24(2):192-203.

Lo WL, Shah NH, Ahsan N, Horkova V, Stepanek O, Salomon AR, Kuriyan J, Weiss A. Lck promotes Zap70-dependent LAT phosphorylation by bridging Zap70 to LAT. Nature Immunology. 2018;19(7):733-41.

Lu YC, Touzjian N, Stenzel M, Dorfman T, Sodroski JG, Haseltine WA. The NF kappa B independent cis-acting sequences in HIV-1 LTR responsive to T-cell activation. Journal of Acquired Immune Deficiency Syndromes. 1991;4(2):173-7.

Maddon PJ, McDougal JS, Clapham PR, Dalgleish AG, Jamal S, Weiss RA, Axel R. HIV infection does not require endocytosis of its receptor, CD4. Cell. 1988;54(6):865-74.

Mahmoudi T, Parra M, Vries RG, Kauder SE, Verrijzer CP, Ott M, Verdin E. The SWI/SNF chromatin-remodeling complex is a cofactor for Tat transactivation of the HIV promoter. The Journal of Biological Chemistry. 2006;281(29):19960-8.

Mali P, Esvelt KM, Church GM. Cas9 as a versatile tool for engineering biology. Nature Methods. 2013;10(10):957-63.

Mali P, Yang L, Esvelt KM, Aach J, Guell M, DiCarlo JE, Norville JE, Church GM. RNA-guided human genome engineering via Cas9. Science. 2013;339(6121):823-6.

Malnati MS, Scarlatti G, Gatto F, Salvatori F, Cassina G, Rutigliano T, Volpi R, Lusso P. A universal real-time PCR assay for the quantification of group-M HIV-1 proviral load. Nature Protocols. 2008;3(7):1240-8.

Martinez RJ, Andargachew R, Martinez HA, Evavold BD. Low-affinity CD4+ T cells are major responders in the primary immune response. Nature Communications. 2016;7:13848.

McDonald D, Wu L, Bohks SM, KewalRamani VN, Unutmaz D, Hope TJ. Recruitment of HIV and its receptors to dendritic cell-T cell junctions. Science. 2003;300(5623):1295-7.

Meier K, Brehm A. Chromatin regulation: how complex does it get. Epigenetics. 2014;9(11):1485-95.

Méndez C, Ledger S, Petoumenos K, Ahlenstiel C, Kelleher AD. RNA-induced epigenetic silencing inhibits HIV-1 reactivation from latency. Retrovirology. 2018;15(1):67.

Miller CM, Akiyama H, Agosto LM, Emery A, Ettinger CR, Swanstrom RI, Henderson AJ, Gummuluru S. Virion-associated Vpr alleviates a postintegration block to HIV-1 infection of dendritic cells. Journal of Virology. 2017;91(13):e00051-17.

Miller JC, Holmes MC, Wang J, Guschin DY, Lee YL, Rupniewski I, Beausejour CM, Waite AJ, Wang NS, Kim KA, Gregory PD, Pabo CO, Rebar EJ. An improved zinc-finger nuclease architecture for highly specific genome editing. Nature Biotechnology. 2007;25(7):778-85.

Miller-Jensen K, Dey SS, Pham N, Foley JE, Arkin AP, Schaffer DV. Chromatin accessibility at the HIV LTR promoter sets a threshold for NF-κB mediated viral gene expression. Integrative Biology: Quantitative Biosciences from Nano to Macro. 2012;4(6):661-71.

Mitsuya H, Weinhold KJ, Furman PA, St Clair MH, Lehrman SN, Gallo RC, Bolognesi D, Barry DW, Broder S. 3'-Azido-3'-deoxythymidine (BW A509U): an antiviral agent that inhibits the infectivity and cytopathic effect of human T-lymphotropic virus type III/lymphadenopathy-associated virus in vitro. Proceedings of the National Academy of Sciences of the United States of America. 1985;82(20):7096-100.

Moosmann P, Georgiev O, Thiesen HJ, Hagmann M, Schaffner W. Silencing of RNA polymerases II and III-dependent transcription by the KRAB protein domain of KOX1, a Krüppel-type zinc finger factor. Biological Chemistry. 1997;378(7):669-77.

Mousseau G, Clementz MA, Bakeman WN, Nagarsheth N, Cameron M, Shi J, Baran P, Fromentin R, Chomont N, Valente ST. An analog of the natural steroidal alkaloid cortistatin A potently suppresses Tat-dependent HIV transcription. Cell Host & Microbe. 2012;12(1):97-108.

Mousseau G, Kessing CF, Fromentin R, Trautmann L, Chomont N, Valente ST. The Tat inhibitor didehydro-cortistatin A prevents HIV-1 reactivation from latency. mBio. 2015;6(4):e00465.

Mout R, Ray M, Lee YW, Scaletti F, Rotello VM. In vivo delivery of CRISPR/Cas9 for therapeutic gene editing: progress and challenges. Bioconjugate Chemistry. 2017;28(4):880-4.

Mussolino C, Morbitzer R, Lütge F, Dannemann N, Lahaye T, Cathomen T. A novel TALE nuclease scaffold enables high genome editing activity in combination with low toxicity. Nucleic Acids Research. 2011;39(21):9283-93.

Napolitano G, Majello B, Licciardo P, Giordano A, Lania L. Transcriptional activity of positive transcription elongation factor b kinase in vivo requires the C-terminal domain of RNA polymerase II. Gene. 2000;254(1-2):139-45.

Natarajan M, August A, Henderson AJ. Combinatorial signals from CD28 differentially regulate human immunodeficiency virus transcription in T cells. The Journal of Biological Chemistry. 2010;285(23):17338-47.

Natarajan M, Schiralli Lester GM, Lee C, Missra A, Wasserman GA, Steffen M, Gilmour DS, Henderson AJ. Negative elongation factor (NELF) coordinates RNA polymerase II pausing, premature termination, and chromatin remodeling to regulate HIV transcription. The Journal of Biological Chemistry. 2013;288(36):25995-6003.

Neri F, Giolo G, Potestà M, Petrini S, Doria M. The HIV-1 Nef protein has a dual role in T cell receptor signaling in infected CD4+ T lymphocytes. Virology. 2011;410(2):316-26.

Neumeister EN, Zhu Y, Richard S, Terhorst C, Chan AC, Shaw AS. Binding of ZAP-70 to phosphorylated T-cell receptor zeta and eta enhances its autophosphorylation and generates specific binding sites for SH2 domain-containing proteins. Molecular and Cellular Biology. 1995;15(6):3171-8.

Nguyen DH, Hildreth JE. Evidence for budding of human immunodeficiency virus type 1 selectively from glycolipid-enriched membrane lipid rafts. Journal of Virology. 2000;74(7):3264-72.

Ocwieja KE, Sherrill-Mix S, Mukherjee R, Custers-Allen R, David P, Brown M, Wang S, Link DR, Olson J, Travers K, Schadt E, Bushman FD. Dynamic regulation of HIV-1 mRNA populations analyzed by single-molecule enrichment and long-read sequencing. Nucleic Acids Research. 2012;40(20):10345-55.

Ogawa S, Watanabe M, Sakurai Y, Inutake Y, Watanabe S, Tai X, Abe R. CD28 signaling in primary CD4(+) T cells: identification of both tyrosine phosphorylation-dependent and phosphorylation-independent pathways. International Immunology. 2013;25(12):671-81.

Ohnishi H, Ledbetter JA, Kanner SB, Linsley PS, Tanaka T, Geller AM, Kotb M. CD28 cross-linking augments TCR-mediated signals and costimulates superantigen responses. Journal of Immunology. 1995;154(7):3180-93.

Okada R, Kondo T, Matsuki F, Takata H, Takiguchi M. Phenotypic classification of human CD4+ T cell subsets and their differentiation. International Immunology. 2008;20(9):1189-99.

Oleksiewicz U, Gładych M, Raman AT, Heyn H, Mereu E, Chlebanowska P, Andrzejewska A, Sozańska B, Samant N, Fąk K, Auguścik P, Kosiński M, Wróblewska JP, Tomczak K, Kulcenty K, Płoski R, Biecek P, Esteller M, Shah PK, Rai K, Wiznerowicz M. TRIM28 and interacting KRAB-ZNFs control self-renewal of human pluripotent stem cells through epigenetic repression of pro-differentiation genes. Stem Cell Reports. 2017;9(6):2065-80.

Oswald-Richter K, Grill SM, Leelawong M, Unutmaz D. HIV infection of primary human T cells is determined by tunable thresholds of T cell activation. European Journal of Immunology. 2004;34(6):1705-14.

Pace MJ, Agosto L, Graf EH, O'Doherty U. HIV reservoirs and latency models. Virology. 2011;411(2):344-54.

Patarca R, Heath C, Goldenberg GJ, Rosen CA, Sodroski JG, Haseltine WA, Hansen UM. Transcription directed by the HIV long terminal repeat in vitro. AIDS Research and Human Retroviruses. 1987;3(1):41-55.

Paul S, Singh AK, Shilpi, Lal G. Phenotypic and functional plasticity of gamma-delta (γδ) T cells in inflammation and tolerance. International Reviews of Immunology. 2014;33(6):537-58.

Pepper M, Jenkins MK. Origins of CD4(+) effector and central memory T cells. Nature Immunology. 2011;12(6):467-71.

Petravic J, Ellenberg P, Chan ML, Paukovics G, Smyth RP, Mak J, Davenport MP. Intracellular dynamics of HIV infection. Journal of Virology. 2014;88(2):1113-24.

Ping YH, Rana TM. DSIF and NELF interact with RNA polymerase II elongation complex and HIV-1 Tat stimulates P-TEFb-mediated phosphorylation of RNA polymerase II and DSIF during transcription elongation. The Journal of Biological Chemistry. 2001;276(16):12951-8.

Pitchenik AE, Fischl MA, Dickinson GM, Becker DM, Fournier AM, O'Connell MT, Colton RM, Spira TJ. Opportunistic infections and Kaposi's sarcoma among Haitians: evidence of a new acquired immunodeficiency state. Annals of Internal Medicine. 1983;98(3):277-84.

Platt RJ, Chen S, Zhou Y, Yim MJ, Swiech L, Kempton HR, Dahlman JE, Parnas O, Eisenhaure TM, Jovanovic M, Graham DB, Jhunjhunwala S, Heidenreich M, Xavier RJ, Langer R, Anderson DG, Hacohen N, Regev A, Feng G, Sharp PA, Zhang F. CRISPR-Cas9 knockin mice for genome editing and cancer modeling. Cell. 2014;159(2):440-55.

Puray-Chavez M, Tedbury PR, Huber AD, Ukah OB, Yapo V, Liu D, Ji J, Wolf JJ, Engelman AN, Sarafianos SG. Multiplex single-cell visualization of nucleic acids and protein during HIV infection. Nature Communications. 2017;8(1):1882.

Purcell DF, Martin MA. Alternative splicing of human immunodeficiency virus type 1 mRNA modulates viral protein expression, replication, and infectivity. Journal of Virology. 1993;67(11):6365-78.

Puryear WB, Akiyama H, Geer SD, Ramirez NP, Yu X, Reinhard BM, Gummuluru S. Interferon-inducible mechanism of dendritic cell-mediated HIV-1 dissemination is dependent on Siglec-1/CD169. PLoS Pathogens. 2013;9(4):e1003291.

Quivy V, De Walque S, Van Lint C. Chromatin-associated regulation of HIV-1 transcription: implications for the development of therapeutic strategies. Sub-cellular Biochemistry. 2007;41:371-96.

Rafati H, Parra M, Hakre S, Moshkin Y, Verdin E, Mahmoudi T. Repressive LTR nucleosome positioning by the BAF complex is required for HIV latency. PLoS Biology. 2011;9(11):e1001206.

Ran FA, Cong L, Yan WX, Scott DA, Gootenberg JS, Kriz AJ, Zetsche B, Shalem O, Wu X, Makarova KS, Koonin EV, Sharp PA, Zhang F. In vivo genome editing using Staphylococcus aureus Cas9. Nature. 2015;520(7546):186-91.

Rankovic S, Varadarajan J, Ramalho R, Aiken C, Rousso I. Reverse transcription mechanically initiates HIV-1 capsid disassembly. Journal of Virology. 2017;91(12):e00289-17.

Razooky BS, Pai A, Aull K, Rouzine IM, Weinberger LS. A hardwired HIV latency program. Cell. 2015;160(5):990-1001.

Rerks-Ngarm S, Pitisuttithum P, Nitayaphan S, Kaewkungwal J, Chiu J, Paris R, Premsri N, Namwat C, de Souza M, Adams E, Benenson M, Gurunathan S, Tartaglia J, McNeil JG, Francis DP, Stablein D, Birx DL, Chunsuttiwat S, Khamboonruang C, Thongcharoen P, Robb ML, Michael NL, Kunasol P, Kim JH, Rerks-Ngarm S, Chunsuttiwat S, Premsri N, Namwat C, Kunasol P, Thongcharoen P, Khamboonruang C, Pitisuttithum P, Bussaratid V, Maek-a-nantawat W, Dhitavat J, Suntharasamai P, Pungpak S, Vanijanonta S, Kaewkunwal J, Khamsiriwatchara A, Jarujareet P, Nitayaphan S, Easmila C, Tabprasit S, Chiu J, Paris R, Benenson M, Brown A, Morgan P, de Souza M, Trichavaroj R, Schuetz A, Thaitawat N, Gurunathan S, Tartaglia J, McNeil JG, Harkness R, Meric C, El Habib R, Baglyos L, Francis D, Lee C, Adams E, Kim JH, Robb ML, Michael NL, Milazzo M, Bolen A, Wessner B, Kim SR, Marovich M, Currier J, Birx DL, Stablein D, Germanson T, Dally L, Wiley R, Excler JL, Berenberg J. Vaccination with ALVAC and AIDSVAX to prevent HIV-1 infection in Thailand. The New England Journal of Medicine. 2009;361(23):2209-20.

Reuse S, Calao M, Kabeya K, Guiguen A, Gatot JS, Quivy V, Vanhulle C, Lamine A, Vaira D, Demonte D, Martinelli V, Veithen E, Cherrier T, Avettand V, Poutrel S, Piette J, de Launoit Y, Moutschen M, Burny A, Rouzioux C, De Wit S, Herbein G, Rohr O, Collette Y, Lambotte O, Clumeck N, Van Lint C. Synergistic activation of HIV-1 expression by deacetylase inhibitors and prostratin: implications for treatment of latent infection. PloS One. 2009;4(6):e6093.

Rhee SG. Regulation of phosphoinositide-specific phospholipase C. Annual Review of Biochemistry. 2001;70:281-312.

Ringler DJ, Hancock WW, King NW, Letvin NL, Daniel MD, Desrosiers RC, Murphy GF. Immunophenotypic characterization of the cutaneous exanthem of SIV-infected rhesus monkeys. Apposition of degenerative Langerhans cells and cytotoxic lymphocytes during the development of acquired immunodeficiency syndrome. The American Journal of Pathology. 1987;126(2):199-207.

Robbez-Masson L, Tie CHC, Conde L, Tunbak H, Husovsky C, Tchasovnikarova IA, Timms RT, Herrero J, Lehner PJ, Rowe HM. The HUSH complex cooperates with TRIM28 to repress young retrotransposons and new genes. Genome Research. 2018;28(6):836-45.

Roche PA, Furuta K. The ins and outs of MHC class II-mediated antigen processing and presentation. Nature Reviews. Immunology. 2015;15(4):203-16.

Rogers PR, Dubey C, Swain SL. Qualitative changes accompany memory T cell generation: faster, more effective responses at lower doses of antigen. Journal of Immunology. 2000;164(5):2338-46.

Romanski A, Uherek C, Bug G, Seifried E, Klingemann H, Wels WS, Ottmann OG, Tonn T. CD19-CAR engineered NK-92 cells are sufficient to overcome NK cell resistance in B-cell malignancies. Journal of Cellular and Molecular Medicine. 2016;20(7):1287-94.

Rossy J, Owen DM, Williamson DJ, Yang Z, Gaus K. Conformational states of the kinase Lck regulate clustering in early T cell signaling. Nature Immunology. 2013;14(1):82-9.

Routy JP, Tremblay CL, Angel JB, Trottier B, Rouleau D, Baril JG, Harris M, Trottier S, Singer J, Chomont N, Sékaly RP, Boulassel MR. Valproic acid in association with highly active antiretroviral therapy for reducing systemic HIV-1 reservoirs: results from a multicentre randomized clinical study. HIV Medicine. 2012;13(5):291-6.

Rowe HM, Jakobsson J, Mesnard D, Rougemont J, Reynard S, Aktas T, Maillard PV, Layard-Liesching H, Verp S, Marquis J, Spitz F, Constam DB, Trono D. KAP1 controls endogenous retroviruses in embryonic stem cells. Nature. 2010;463(7278):237-40.

Ruelas DS, Greene WC. An integrated overview of HIV-1 latency. Cell. 2013;155(3):519-29.

Saad JS, Miller J, Tai J, Kim A, Ghanam RH, Summers MF. Structural basis for targeting HIV-1 Gag proteins to the plasma membrane for virus assembly. Proceedings of the National Academy of Sciences of the United States of America. 2006;103(30):11364-9.

Saayman SM, Lazar DC, Scott TA, Hart JR, Takahashi M, Burnett JC, Planelles V, Morris KV, Weinberg MS. Potent and targeted activation of latent HIV-1 using the CRISPR/dCas9 activator complex. Molecular Therapy. 2016;24(3):488-98.

Sagot-Lerolle N, Lamine A, Chaix ML, Boufassa F, Aboulker JP, Costagliola D, Goujard C, Pallier C, Paller C, Delfraissy JF, Lambotte O. Prolonged valproic acid treatment does not reduce the size of latent HIV reservoir. AIDS. 2008;22(10):1125-9.

Saleh S, Solomon A, Wightman F, Xhilaga M, Cameron PU, Lewin SR. CCR7 ligands CCL19 and CCL21 increase permissiveness of resting memory CD4+ T cells to HIV-1 infection: a novel model of HIV-1 latency. Blood. 2007;110(13):4161-4.

Saleh S, Lu HK, Evans V, Harisson D, Zhou J, Jaworowski A, Sallmann G, Cheong KY, Mota TM, Tennakoon S, Angelovich TA, Anderson J, Harman A, Cunningham A, Gray L, Churchill M, Mak J, Drummer H, Vatakis DN, Lewin SR, Cameron PU. HIV integration and the establishment of latency in CCL19-treated resting CD4(+) T cells require activation of NF-κB. Retrovirology. 2016;13(1):49.

Santos ASEAC, Silveira EAD, Falco MO, Nery MW, Turchi MD. Effectiveness of nutritional treatment and synbiotic use on gastrointestinal symptoms reduction in HIV-infected patients: Randomized clinical trial. Clinical Nutrition. 2017;36(3):680-5.

Sauter D, Kirchhoff F. Key Viral Adaptations Preceding the AIDS Pandemic. Cell Host & Microbe. 2019;25(1):27-38.

Sauter D, Schindler M, Specht A, Landford WN, Münch J, Kim KA, Votteler J, Schubert U, Bibollet-Ruche F, Keele BF, Takehisa J, Ogando Y, Ochsenbauer C, Kappes JC, Ayouba A, Peeters M, Learn GH, Shaw G, Sharp PM, Bieniasz P, Hahn BH, Hatziioannou T, Kirchhoff F. Tetherin-driven adaptation of Vpu and Nef function and the evolution of pandemic and nonpandemic HIV-1 strains. Cell Host & Microbe. 2009;6(5):409-21.

Schier R, McCall A, Adams GP, Marshall KW, Merritt H, Yim M, Crawford RS, Weiner LM, Marks C, Marks JD. Isolation of picomolar affinity anti-c-erbB-2 single-chain Fv by molecular evolution of the complementarity determining regions in the center of the antibody binding site. Journal of Molecular Biology. 1996;263(4):551-67.

Schiralli Lester GM, Akiyama H, Evans E, Singh J, Gummuluru S, Henderson AJ. Interleukin 2-inducible T cell kinase (ITK) facilitates efficient egress of HIV-1 by coordinating Gag distribution and actin organization. Virology. 2013;436(1):235-43.

Sette P, O'Connor SK, Yerramilli VS, Dussupt V, Nagashima K, Chutiraka K, Lingappa J, Scarlata S, Bouamr F. HIV-1 nucleocapsid mimics the membrane adaptor syntenin PDZ to gain access to ESCRTs and promote virus budding. Cell Host & Microbe. 2016;19(3):336-48.

Seu L, Sabbaj S, Duverger A, Wagner F, Anderson JC, Davies E, Wolschendorf F, Willey CD, Saag MS, Goepfert P, Kutsch O. Stable phenotypic changes of the host T

cells are essential to the long-term stability of latent HIV-1 infection. Journal of Virology. 2015;89(13):6656-72.

Shearer GM, Bernstein DC, Tung KS, Via CS, Redfield R, Salahuddin SZ, Gallo RC. A model for the selective loss of major histocompatibility complex self-restricted T cell immune responses during the development of acquired immune deficiency syndrome (AIDS). Journal of Immunology. 1986;137(8):2514-21.

Shen A, Zink MC, Mankowski JL, Chadwick K, Margolick JB, Carruth LM, Li M, Clements JE, Siliciano RF. Resting CD4+ T lymphocytes but not thymocytes provide a latent viral reservoir in a simian immunodeficiency virus-Macaca nemestrina model of human immunodeficiency virus type 1-infected patients on highly active antiretroviral therapy. Journal of Virology. 2003;77(8):4938-49.

Siliciano JD, Siliciano RF. Enhanced culture assay for detection and quantitation of latently infected, resting CD4+ T-cells carrying replication-competent virus in HIV-1-infected individuals. Methods in Molecular Biology. 2005;304:3-15.

Simioni S, Cavassini M, Annoni JM, Rimbault Abraham A, Bourquin I, Schiffer V, Calmy A, Chave JP, Giacobini E, Hirschel B, Du Pasquier RA. Cognitive dysfunction in HIV patients despite long-standing suppression of viremia. AIDS. 2010;24(9):1243-50.

Smith TF, Srinivasan A, Schochetman G, Marcus M, Myers G. The phylogenetic history of immunodeficiency viruses. Nature. 1988;333(6173):573-5.

Smith-Garvin JE, Koretzky GA, Jordan MS. T cell activation. Annual Review of Immunology. 2009;27:591-619.

Sommermeyer D, Hudecek M, Kosasih PL, Gogishvili T, Maloney DG, Turtle CJ, Riddell SR. Chimeric antigen receptor-modified T cells derived from defined CD8+ and CD4+ subsets confer superior antitumor reactivity in vivo. Leukemia. 2016;30(2):492-500.

Soriano-Sarabia N, Archin NM, Bateson R, Dahl NP, Crooks AM, Kuruc JD, Garrido C, Margolis DM. Peripheral Vγ9Vδ2 T cells are a novel reservoir of latent HIV infection. PLoS pathogens. 2015;11(10):e1005201.

Sowd GA, Serrao E, Wang H, Wang W, Fadel HJ, Poeschla EM, Engelman AN. A critical role for alternative polyadenylation factor CPSF6 in targeting HIV-1 integration to transcriptionally active chromatin. Proceedings of the National Academy of Sciences of the United States of America. 2016;113(8):E1054-63.

Steffens CM, Managlia EZ, Landay A, Al-Harthi L. Interleukin-7-treated naive T cells can be productively infected by T-cell-adapted and primary isolates of human immunodeficiency virus 1. Blood. 2002;99(9):3310-8.

Stevenson M, Stanwick TL, Dempsey MP, Lamonica CA. HIV-1 replication is controlled at the level of T cell activation and proviral integration. The EMBO Journal. 1990;9(5):1551-60.

Stoltzfus CM. Chapter 1. Regulation of HIV-1 alternative RNA splicing and its role in virus replication. Advances in virus research. 2009;74:1-40.

Stover J, Bollinger L, Izazola JA, Loures L, DeLay P, Ghys PD. What is required to end the AIDS epidemic as a public health threat by 2030? The cost and impact of the fast-track approach. PloS One. 2016;11(5):e0154893.

Stuart RM, Grobicki L, Haghparast-Bidgoli H, Panovska-Griffiths J, Skordis J, Keiser O, Estill J, Baranczuk Z, Kelly SL, Reporter I, Kedziora DJ, Shattock AJ, Petravic J, Hussain SA, Grantham KL, Gray RT, Yap XF, Martin-Hughes R, Benedikt CJ, Fraser-Hurt N, Masaki E, Wilson DJ, Gorgens M, Mziray E, Cheikh N, Shubber Z, Kerr CC, Wilson DP. How should HIV resources be allocated? Lessons learnt from applying Optima HIV in 23 countries. Journal of the International AIDS Society. 2018;21(4):e25097.

Sundquist WI, Kräusslich HG. HIV-1 assembly, budding, and maturation. Cold Spring Harbor Perspectives in Medicine. 2012;2(7):a006924.

Swanstrom R, Wills JW. Synthesis, assembly, and processing of viral proteins. In Retroviruses, eds.Coffin JM, Hughes SH, Varmus HE. Cold Spring Harbor, NY: Cold Spring Harbor Press; 1997.

Swiggard WJ, Baytop C, Yu JJ, Dai J, Li C, Schretzenmair R, Theodosopoulos T, O'Doherty U. Human immunodeficiency virus type 1 can establish latent infection in resting CD4+ T cells in the absence of activating stimuli. Journal of Virology. 2005;79(22):14179-88.

Thakore PI, D'Ippolito AM, Song L, Safi A, Shivakumar NK, Kabadi AM, Reddy TE, Crawford GE, Gersbach CA. Highly specific epigenome editing by CRISPR-Cas9 repressors for silencing of distal regulatory elements. Nature Methods. 2015;12(12):1143-9.

Thierry S, Marechal V, Rosenzwajg M, Sabbah M, Redeuilh G, Nicolas JC, Gozlan J. Cell cycle arrest in G2 induces human immunodeficiency virus type 1 transcriptional activation through histone acetylation and recruitment of CBP, NF-kappaB, and c-Jun to the long terminal repeat promoter. Journal of Virology. 2004;78(22):12198-206.

Tisdale M, Kemp SD, Parry NR, Larder BA. Rapid in vitro selection of human immunodeficiency virus type 1 resistant to 3'-thiacytidine inhibitors due to a mutation in the YMDD region of reverse transcriptase. Proceedings of the National Academy of Sciences of the United States of America. 1993;90(12):5653-6.

UNAIDS. Global HIV & AIDS Statistics – 2018 Fact Sheet. http://www.unaids.org/en/resources/fact-sheet. Accessed February 8, 2019.

UNAIDS. Guidance Note on HIV and Sex Work. http://www.unaids.org/en/resources/documents/2012/20120402_UNAIDS-guidance-note-HIV-sex-work. Accessed February 8, 2019.

University of Michigan, Molecular and Behavioral Neuroscience Institute. Brainarray. http://brainarray.mbni.med.umich.edu/Brainarray/Database/CustomCDF. Accessed February 16, 2019.

Van Lint C, Bouchat S, Marcello A. HIV-1 transcription and latency: an update. Retrovirology. 2013;10:67.

Van Lint C, Emiliani S, Ott M, Verdin E. Transcriptional activation and chromatin remodeling of the HIV-1 promoter in response to histone acetylation. The EMBO Journal. 1996;15(5):1112-20.

Verdin E, Paras P, Van Lint C. Chromatin disruption in the promoter of human immunodeficiency virus type 1 during transcriptional activation. The EMBO Journal. 1993;12(8):3249-59.

von Boehmer H, Kisielow P. Self-nonself discrimination by T cells. Science. 1990;248(4961):1369-73.

Wang G, Zhao N, Berkhout B, Das AT. CRISPR-Cas9 can inhibit HIV-1 replication but NHEJ repair facilitates virus escape. Molecular Therapy: The Journal of the American Society of Gene Therapy. 2016;24(3):522-6.

Wang GP, Ciuffi A, Leipzig J, Berry CC, Bushman FD. HIV integration site selection: analysis by massively parallel pyrosequencing reveals association with epigenetic modifications. Genome Research. 2007;17(8):1186-94.

Wang H, Cohen AA, Galimidi RP, Gristick HB, Jensen GJ, Bjorkman PJ. Cryo-EM structure of a CD4-bound open HIV-1 envelope trimer reveals structural rearrangements of the gp120 V1V2 loop. Proceedings of the National Academy of Sciences of the United States of America. 2016;113(46):E7151-E7158.

Wang JH, Reinherz EL. Structural basis of T cell recognition of peptides bound to MHC molecules. Molecular Immunology. 2002;38(14):1039-49.

Wang Z, Gurule EE, Brennan TP, Gerold JM, Kwon KJ, Hosmane NN, Kumar MR, Beg SA, Capoferri AA, Ray SC, Ho YC, Hill AL, Siliciano JD, Siliciano RF. Expanded cellular clones carrying replication-competent HIV-1 persist, wax, and wane. Proceedings of the National Academy of Sciences of the United States of America. 2018;115(11):E2575-E2584.

Wang Z, Pan Q, Gendron P, Zhu W, Guo F, Cen S, Wainberg MA, Liang C. CRISPR/Cas9-derived mutations both inhibit HIV-1 replication and accelerate viral escape. Cell Reports. 2016;15(3):481-9.

Weinberger LS, Burnett JC, Toettcher JE, Arkin AP, Schaffer DV. Stochastic gene expression in a lentiviral positive-feedback loop: HIV-1 Tat fluctuations drive phenotypic diversity. Cell. 2005;122(2):169-82.

Whitney JB, Hill AL, Sanisetty S, Penaloza-MacMaster P, Liu J, Shetty M, Parenteau L, Cabral C, Shields J, Blackmore S, Smith JY, Brinkman AL, Peter LE, Mathew SI, Smith KM, Borducchi EN, Rosenbloom DI, Lewis MG, Hattersley J, Li B, Hesselgesser J, Geleziunas R, Robb ML, Kim JH, Michael NL, Barouch DH. Rapid seeding of the viral reservoir prior to SIV viraemia in rhesus monkeys. Nature. 2014;512(7512):74-7.

Williams SA, Chen LF, Kwon H, Ruiz-Jarabo CM, Verdin E, Greene WC. NF-kappaB p50 promotes HIV latency through HDAC recruitment and repression of transcriptional initiation. The EMBO Journal. 2006;25(1):139-49.

Williams SA, Kwon H, Chen LF, Greene WC. Sustained induction of NF-kappa B is required for efficient expression of latent human immunodeficiency virus type 1. Journal of virology. 2007;81(11):6043-56.

Wolf D, Goff SP. Embryonic stem cells use ZFP809 to silence retroviral DNAs. Nature. 2009;458(7242):1201-4.

Wolf G, Yang P, Füchtbauer AC, Füchtbauer EM, Silva AM, Park C, Wu W, Nielsen AL, Pedersen FS, Macfarlan TS. The KRAB zinc finger protein ZFP809 is required to initiate epigenetic silencing of endogenous retroviruses. Genes & Development. 2015;29(5):538-54.

Wong JK, Hezareh M, Günthard HF, Havlir DV, Ignacio CC, Spina CA, Richman DD. Recovery of replication-competent HIV despite prolonged suppression of plasma viremia. Science. 1997;278(5341):1291-5.

Wu PY, Cheng CY, Liu CE, Lee YC, Yang CJ, Tsai MS, Cheng SH, Lin SP, Lin DY, Wang NC, Lee YC, Sun HY, Tang HJ, Hung CC. Multicenter study of skin rashes and hepatotoxicity in antiretroviral-naïve HIV-positive patients receiving non-

nucleoside reverse-transcriptase inhibitor plus nucleoside reverse-transcriptase inhibitors in Taiwan. PloS One. 2017;12(2):e0171596.

Xie H, Tang L, He X, Liu X, Zhou C, Liu J, Ge X, Li J, Liu C, Zhao J, Qu J, Song Z, Gu F. SaCas9 requires 5'-NNGRRT-3' PAM for sufficient cleavage and possesses higher cleavage activity than SpCas9 or FnCpf1 in human cells. Biotechnology Journal. 2018;13(4):e1700561.

Xing S, Siliciano RF. Targeting HIV latency: pharmacologic strategies toward eradication. Drug Discovery Today. 2013;18(11-12):541-51.

Yamanaka Y, Friess H, Kobrin MS, Büchler M, Kunz J, Beger HG, Korc M. Overexpression of HER2/neu oncogene in human pancreatic carcinoma. Human Pathology. 1993;24(10):1127-34.

Yang Z, Zhu Q, Luo K, Zhou Q. The 7SK small nuclear RNA inhibits the CDK9/cyclin T1 kinase to control transcription. Nature. 2001;414(6861):317-22.

Yuan Z, Fan X, Staitieh B, Bedi C, Spearman P, Guidot DM, Sadikot RT. HIV-related proteins prolong macrophage survival through induction of Triggering receptor expressed on myeloid cells-1. Scientific Reports. 2017;7:42028.

Yukl SA, Kaiser P, Kim P, Telwatte S, Joshi SK, Vu M, Lampiris H, Wong JK. HIV latency in isolated patient CD4+ T cells may be due to blocks in HIV transcriptional elongation, completion, and splicing. Science Translational Medicine. 2018;10(430):eaap9927.

Ylisastigui L, Archin NM, Lehrman G, Bosch RJ, Margolis DM. Coaxing HIV-1 from resting CD4 T cells: histone deacetylase inhibition allows latent viral expression. AIDS. 2004;18(8):1101-8.

Zehn D, Lee SY, Bevan MJ. Complete but curtailed T-cell response to very low-affinity antigen. Nature. 2009;458(7235):211-4.

Zerihun MB, Vaillant C, Jost D. Effect of replication on epigenetic memory and consequences on gene transcription. Physical Biology. 2015;12(2):026007.

Zetsche B, Volz SE, Zhang F. A split-Cas9 architecture for inducible genome editing and transcription modulation. Nature Biotechnology. 2015;33(2):139-42.

Zhang Y, Yin C, Zhang T, Li F, Yang W, Kaminski R, Fagan PR, Putatunda R, Young WB, Khalili K, Hu W. CRISPR/gRNA-directed synergistic activation mediator (SAM) induces specific, persistent and robust reactivation of the HIV-1 latent reservoirs. Scientific Reports. 2015;5:16277.

Zhang Z, Klatt A, Gilmour DS, Henderson AJ. Negative elongation factor NELF represses human immunodeficiency virus transcription by pausing the RNA polymerase II complex. The Journal of Biological Chemistry. 2007;282(23):16981-8.

Zhang Z, Klatt A, Henderson AJ, Gilmour DS. Transcription termination factor Pcf11 limits the processivity of Pol II on an HIV provirus to repress gene expression. Genes & Development. 2007;21(13):1609-14.

Zhao Y, Lei M, Wang Z, Qiao G, Yang T, Zhang J. TCR-induced, PKC-θ-mediated NF-κB activation is regulated by a caspase-8-caspase-9-caspase-3 cascade. Biochemical and Biophysical Research Communications. 2014;450(1):526-31.

Zhou Q, Yik JH. The Yin and Yang of P-TEFb regulation: implications for human immunodeficiency virus gene expression and global control of cell growth and differentiation. Microbiology and Molecular Biology Reviews. 2006;70(3):646-59.

Zhu J, Gaiha GD, John SP, Pertel T, Chin CR, Gao G, Qu H, Walker BD, Elledge SJ, Brass AL. Reactivation of latent HIV-1 by inhibition of BRD4. Cell Reports. 2012;2(4):807-16.

Zhu P, Liu J, Bess J, Chertova E, Lifson JD, Grisé H, Ofek GA, Taylor KA, Roux KH. Distribution and three-dimensional structure of AIDS virus envelope spikes. Nature. 2006;441(7095):847-52.

Zikherman J, Au-Yeung B. The role of T cell receptor signaling thresholds in guiding T cell fate decisions. Current Opinion in Immunology. 2015;33:43-8.

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